AM
1938
fri

Friedman,R.S.

NATIONAL
E74-21268

BOSTON UNIVERSITY

GRADUATE SCHOOL

Thesis

TERATOLOGY OF THE HUMAN FEMALE GENITALIA

by

Robert Simon Friedman

(B.S. in Ed., Boston University School of Education, 1936)

submitted in partial fulfilment of the
requirements for the degree of
Master of Arts

1938

AM
1938
fr1

CONTENTS

Introduction .... Page 1.
The Anatomy of the Female Genitalia .... 5.
Ovaries .... 5.
Fallopian Tubes .... 6.
Uterus .... 8.
Vagina .... 9.
Hymen .... 9.
External Genitals .... 10.
The Embryology of the Genitalia .... 16.
The Anomalies of the Female Genitalia ..... 22.
Ovaries .... 22.
Fallopian Tubes .... 27.
Uterus .... 30.
Vagina .... 43.
Hymen .... 45.
External Genitals .... 50.
Hermaphroditism .... 53.
The Embryology of Genital Anomalies .... 55.
Causative Factors of Genital Anomalies .... 59.
Correlation of the Causative Factors ...... 80.
Summary .... 83.

Bibliography.

CONTENTS

Introduction .... Page 1.

The Anatomy of the Female Genitalia .... 5.

- Ovaries .... 5.
- Fallopian Tubes .... 6.
- Uterus .... 8.
- Vagina .... 9.
- Hymen .... 9.
- External Genitals .... 10.

The Embryology of the Genitalia .... 15.

The Anomalies of the Female Genitalia ..... 22.

- Ovaries .... 22.
- Fallopian Tubes .... 27.
- Uterus .... 30.
- Vagina .... 43.
- Hymen .... 45.
- External Genitals .... 50.
- Hermaphroditism .... 53.

The Embryology of Genital Anomalies .... 55.

Causative Factors of Genital Anomalies .... 60.

Correlation of the Causative Factors ...... 80.

Summary .... 83.

Bibliography.

ILLUSTRATIONS

The Internal Genitals .... Page 13.

The Internal Genitals --- Sagittal View ... 14.

Uterine Forms .... 37.

Uterine Forms .... 38.

Digitized by the Internet Archive
in 2016 with funding from
Boston Library Consortium Member Libraries

https://archive.org/details/teratologyofhuma00frie

INTRODUCTION

This paper is a discussion of the congenital morphological anomalies of the female genital organs, primarily with relation to human beings.

The anatomical description of the principal forms of genital abnormalities has been augmented by a discussion, criticism, and correlative interpretation of the three foremost suggested causative factors of the malformations.

Anomalous conditions arising from irritations and inflammations caused by diseases, either acquired or inherited, have been strictly avoided.

In the main, the material for this paper has been gathered from the literature of the workers in the various fields which the subject embraces, as well as from the secondary sources of authorities on female genital malformations.

However, the intention has been to extend the scope

INTRODUCTION

This paper is a discussion of the congenital morphological anomalies of the female genital organs, primarily with relation to human beings.

The anatomical description of the principal forms of genital abnormalities has been augmented by a discussion, criticism, and correlative interpretation of the three foremost suggested causative factors of the malformations.

Anomalous conditions arising from irritations and inflammations caused by diseases, either acquired or inherited, have been strictly avoided.

In the main, the material for this paper has been gathered from the literature of the workers in the various fields which the subject embraces, as well as from the secondary sources of authorities on female genital malformations.

However, the intention has been to extend the scope

of the work beyond the mere compilation of facts and hypotheses. A vast quantity of literature has been produced on the subject of abnormal forms of the reproductive organs. Much of the material has been rendered obsolete by recent findings. Many of the theories concerning the causes are unfounded fancies, some are pseudoscientific perversions of fact, while still others are misinterpretations of evidence, or conclusions based on inadequate information. Actualities are almost obscured by the confusing array of claims advanced by all types from the workers of Black Magic to overzealous but too narrow-visioned students.

An attempt has been made to make a scientific evaluation of the available material, and to discriminate between the plausible and the improbable, with the ultimate intention of presenting only pertinent and valid information.

Once the material had been selected and organized, there seemed to be an apparent connection between the heretofore segregated causative factors. Hence, the endeavor has been made to correlate the causes and to indicate their interdependence.

Since the paper is intended as a comprehensive study of the genital malformations of females, the rigid restriction of subject matter to anomalies exclusively, would be inadequate. The main topic is dependent on the sciences of anatomy, embryology, and genetics, and also embraces several of the work beyond the mere compilation of facts and hypotheses. A vast quantity of literature has been produced on the subject of abnormal forms of the reproductive organs. Much of the material has been rendered obsolete by recent findings. Many of the theories concerning the causes are unfounded fancies, some are pseudoscientific perversions of fact, while still others are misinterpretations of evidence, or conclusions based on inadequate information. Actualities are almost obscured by the confusing array of claims advanced by all types from the workers of Black Magic to overzealous but too narrow-visioned students.

An attempt has been made to make a scientific evaluation of the available material, and to discriminate between the plausible and the improbable, with the ultimate intention of presenting only pertinent and valid information.

Once the material had been selected and organized, there seemed to be an apparent connection between the heretofore segregated causative factors. Hence, the endeavor has been made to correlate the causes and to indicate their interdependence.

Since the paper is intended as a comprehensive study of the genital malformations of females, the rigid restriction of subject matter to anomalies exclusively, would be inadequate. The main topic is dependent on the sciences of anatomy, embryology, and genetics, and also embraces several aspects of physiology. Therefore, it seemed necessary and logical to devote attention to the normal manifestations of these fields, in so far as they constitute a pertinent background for the principal theme. With this belief in mind, the arrangement and inclusions have been organized as follows:

The first section of the paper consists of a treatment of the normal anatomy of the reproductive organs. This inclusion is made on the contention that a comprehension of the normal is essential to an adequate understanding and appreciation of the various deviations from the normal.

Inasmuch as the embryological processes involved constitute such an important factor in the explanation of the defects, it has been deemed advisable to outline the normal course of organ development.

The third main division of the paper describes the anomalous conditions of the genitalia. In a few instances, the anatomical exposition has been augmented by the account of detailed causes of particular interest or importance. A more generalized explanation of the occurrence of the genital malformations is presented under the section dealing with the deviations from the normal embryological course. A knowledge of the embryology of the genitals serves to organize the abnormalities and indicates their logical interrelation.

The final portion of the thesis presents the fundamental causative factors of the anomalies of the reproductive system. In addition to including the substantiating arguments

and evidence for the three most generally accepted causes, an attempt has been made to correlate the suggested causes and to show their mutual interdependence and interrelation.

THE ANATOMY OF THE
FEMALE GENITALIA

The female reproductive system in human beings consists of two egg-producing glands, the *ovaries*, at the innermost extremity. Next are the two *Fallopian tubes* or *oviducts*, which carry the eggs in their physiological migration. A single *uterus* or *womb* receives the eggs from the oviducts and acts as a chamber for the incubation of the fertilized eggs and for the excretion of the impregnant eggs. External to the uterus is a canal used for copulation and for the expulsion of the neonate and the eggs. This canal is the *vagina*. At the outermost extremity is the vestibule of the urogenital system, the *vulva*. In human beings, the vulva acts as a region of sexual sensibility. (16)

OVARIES

The two ovaries lie against the side wall of the pelvic cavity, symmetrically on each side of the uterus. Their usual location is in the *ovarian fossa of Krause*--a depression separating the obliterated umbilical artery from the hypogastric vein. (13) The ovary is suspended in the pelvic cavity by a peritoneal fold and by ligaments. Above, it is hung from the *suspensory ligament of the ovary*, which is a

peritoneal fold that joins the peritoneum covering the psoas major muscle. At its internal extremity, the gland is attached to the utero-ovarian ligament which in turn joins the superior portion of the uterus. An enlarged process from the fimbriated extremity of the oviduct known as the ovarian fimbria connects the lateral portion of the ovary with the beginning of the Fallopian tube. Below, the ovary is attached to a large peritoneum, the broad ligament. (13, 16)

The ovary has about the size and shape of a large almond. Approximate average measurements place its length and width at 40 mm. and 18 mm. respectively. Its thickness rarely exceeds 14 mm.. The superior or external extremity is slightly rounded, and the inferior extremity, to which the utero-ovarian ligament is attached, is pointed. The gross external appearance before puberty is smooth, but after menstruation starts the surface acquires a roughened appearance, and one or more transparent fluid-filled vesicles may be present in the adult ovary. (13, 16)

FALLOPIAN TUBES

The oviduct is a hollow tube that connects the glands to the uterus. Its length varies from 10 to 15 cm.. The outside diameter decreases from a maximum of 7 mm. at the glandular extremity to 3 mm. at the internal segment where the Fallopian tube enters the uterus. The lumen of the ducts undergoes a similar decrease in diameter. The Fallopian tubes

are divided into five sections, the pavilion, the ampulla, the isthmus, and the parietal portion.

The pavilion, also known as the infundibulum or the fimbriated extremity, is a funnel-shaped opening that is divided into denticulations which hang into the abdominal cavity. There may be twelve to fifteen of these fringes present. It is one of these fimbriae that becomes enlarged to form the ovarian fimbria or tubo-ovarian ligament. At the bottom of the funnel is a 2 mm. orifice, the abdominal ostium.

The pavilion leads to the intermediate segment of the oviduct known as the ampulla. The ampulla is approximately 7 cm. long and has an average diameter of 7 mm.. However, its course is flexuose and it is often constricted in some parts and distended in others. The internal end of the ampulla tapers in suddenly to join the narrower portion of the Fallopian tube, which is termed the isthmus. This fourth segment has thicker walls than the ampulla, but possesses a much finer lumen. Its length is about 4 cm., and it is 3 mm. in diameter. The isthmus is the innermost section of the abdominal portion of the oviduct.

The fifth and final portion, the parietal or pars uterina, lies in the wall of the uterus at the latero-superior angle of that organ. Its length is about 3 cm., which is the thickness of the wall of the uterus. The pars uterina terminates in the uterine orifice, an ostium slightly

smaller in diameter than the abdominal orifice.

It is significant to note that there is no definite ductular connection to conduct the eggs from the ovary to the pavilion of the Fallopian tube.

UTERUS

The uterus is a hollow, thick-walled, muscular organ occupying the pelvic cavity between the rectum and the bladder. This pear-shaped body projects cranio-ventrad. Its anterior surface is nearly plane, but its posterior aspect is definitely convex. The uterus averages 7½ cm. in length, and is about 5 cm. wide at its upper part, but tapers gradually to a somewhat smaller width caudally. Its depth of 2½ cm. remains approximately uniform throughout its length.

The cranial end of the uterus is a large, somewhat rounded surface known as the _fundus_. The insertion of the Fallopian tubes into the uterus forms the line of demarcation between the fundus and the _body_, or _corpus uteri_. The body consists of the upper two-thirds to three-fourths of the entire organ. There is usually a constriction or a sudden tapering at the lower end of the body which marks the beginning of the external portion, the _cervix_, or _neck of the uterus_. The lumen at the point of separation has been termed the _internal orifice_.

The cylindrical cervix, which is about an inch long, is divided into a _supravaginal_ and a _vaginal_ portion. The line

of separation is formed by the circular insertion of the vagina. The vaginal portion projects dorso-caudally through the upper part of the anterior wall of the vagina, and terminates with the external orifice of the uterus which is surrounded by an anterior and a posterior lip. The anterior lip is thicker and more rounded, while the posterior lip is the longer and thinner.

In addition to the slight anteversion of the uterus which causes it to form an obtuse angle with the vagina, the organ usually has a minor lateroversion to the left. (13, 16)

VAGINA

Connected to the uterus is the musculo-membranous copulating pouch, the vagina. This organ, the length of which is approximately the same as that of the uterus, projects ventro-caudad from its junction with the cervix uteri. The lumen of the vagina is practically obscured by numerous longitudinal folds. However, the folds and the muscular walls of the organ are very elastic and are capable of considerable dilation. (13, 16)

HYMEN

Separating the external extremity of the genital canal from the uro-genital vestibule is a tissue fold from the vulvo-vaginal mucous membrane. This structure, the hymen, is a membrane composed of connective tissue, elastic tissue,

nerves, and a more or less liberal vascular network. The proportions of the different constituents vary considerably, as does the thickness and shape of the membrane. The shape of the hymeneal perforation normally assumes one of three types. First, and most frequent in occurrence, is the crescent or semilunar hymen. This type is a crescent-shaped slit whose ends taper antero-laterally. The anterior border is concave, and the posterior border is sharply convex. The main part of the aperture lies toward the anterior part of the membrane.

Second is the annular or diaphragmatic type of hymen. Here, the opening appears as a somewhat circular perforation, of varying diameter, lying at or near the center of the hymen.

The third common type is the linear or labiate. This modification presents an antero-posterior slit bordered laterally by two more or less fringed lips.

There are a great variety of additional types of hymeneal apertures, ranging from slight deviations of the above three forms, to anomalous conditions that cause serious physiological complications. (16, 55, 13)

EXTERNAL GENITALS

Finally, at the external extremity of the genital canal there is the vulva with its associated parts, the labia majora, the labia minora, the clitoris, and the mons veneris. The vulva is an antero-posterior fissure some 6 or 7 cm. long that

opens to the outside of the body. Internally there is a shallow infundibuliform cavity leading to the opening of the vagina and the urethra.

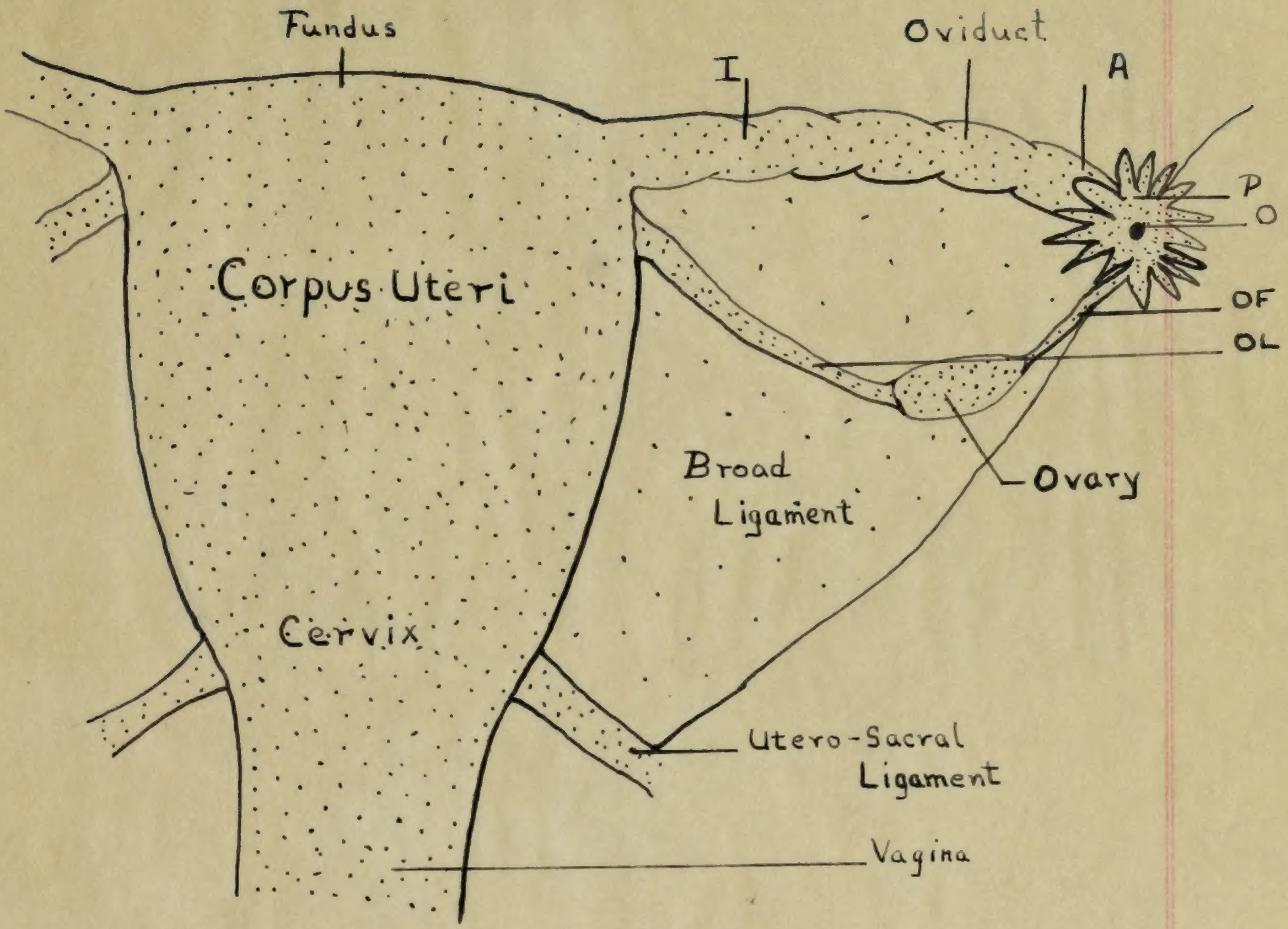
Running longitudinally along the lateral borders of the vulvar slit, at the external extremity, is a pair of rounded cutaneous folds, the labia majora. They originate from a medial point on the perineum, behind the vulva, and become enlarged as they pass forward to fuse anteriorly at the mid-point in the triangular prominence of adipose and cutaneous tissue known as the mons veneris (also mons pubis, or anterior commissure.)

Running somewhat parallel to the labia majora on their inner surfaces is a pair of thinner, smaller folds, resembling mucous membranes, which are the labia minora. Like the labia majora, the labia minora exhibit a decrease in size toward their posterior ends. At this hind point, the two inner labia fuse with the posterior portions of the labia majora.

On the roof of the vulvar vestibule is a small projection (2½ to 4 cm. in length) composed of erectile tissue, which is the morphological equivalent of the penis. And like the penis, this organ, the clitoris, has a small hood of very sensitive erectile tissue, the glans clitoridis, covering its distal end.

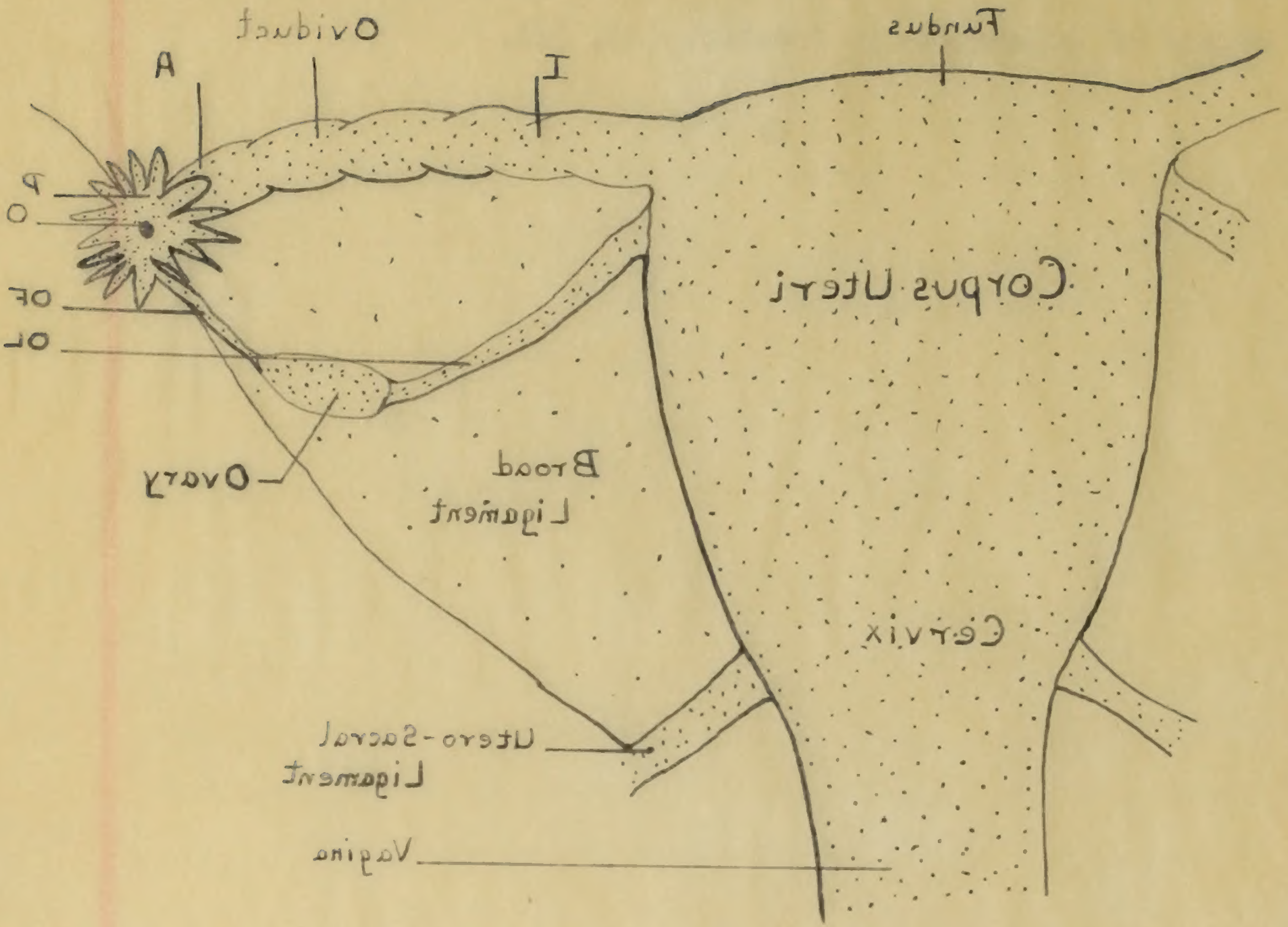
A pair of erectile organs situated lateral to the vestibule, the bulbs of the vulva, and the racemose glands of Bartholin, whose ducts open into the sides of the vestibule

to secrete the female ejaculatory fluid complete the main organs of generation in females. (13, 16).


Fundus
I
Oviduct
A
P
O
OF
OL
Corpus Uteri
Broad Ligament
Ovary
Cervix
Utero-Sacral Ligament
Vagina

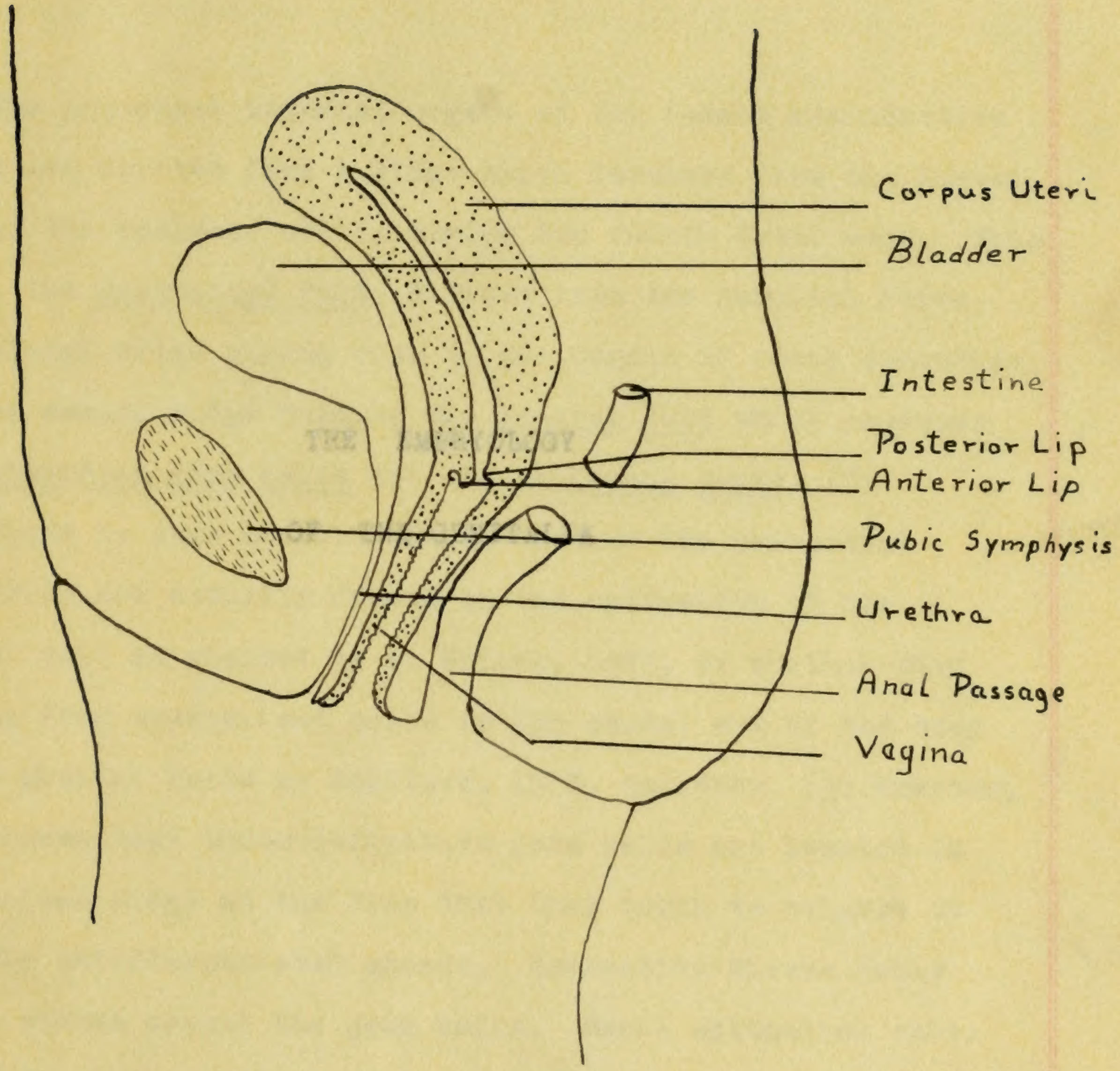
I = Isthmus
A = Ampulla
P = Fimbriated Extremity
O = Abdominal Ostium
OF = Ovarian Fimbria
OL = Ovarian Ligament

I. - THE INTERNAL GENITALS - Ventral Surface


Oviduct
A
I
Fundus
P
O
OF
OL
Corpus Uteri
Broad Ligament
Ovary
Cervix
Utero-Sacral Ligament
Vagina

I = Isthmus
A = Ampulla
P = Fimbriated Extremity
O = Abdominal Ostium
OF = Ovarian Fimbria
OL = Ovarian Ligament

I. - THE INTERNAL GENITALS - ventral surface


Corpus Uteri
Bladder
Intestine
Posterior Lip
Anterior Lip
Pubic Symphysis
Urethra
Anal Passage
Vagina

II. - THE INTERNAL GENITALS — Saqittal View.

(After Cunningham)

THE EMBRYOLOGY
OF THE GENITALIA

The principal internal organs of the female reproductive system are derived from a ridge which develops from the dorsal wall of the coelomic cavity during the fourth fetal week. This ridge, the urogenital fold, divides into two parallel folds, the lateral ridge giving rise to the organs of renal excretion, and the medial ridge forming the genital fold which produces the primordial germ cells and the Müllerian ducts. (3)

There is some question as to whether the primordial germ cells are actually formed in the epithelium of the genital fold as claimed by H. Stieve, 1927, or whether they migrate from specialized cells in the caudal end of the body to the genital folds as Politzer, 1928, believes. (3) However, it is known that these definitive germ cells are located in the genital ridge at the time that they begin to enlarge to form the undifferentiated gonads. Connective tissue cells form a stroma around the germ cells. Small epithelial cells surround a larger cell producing a primordial ovum with its membrana granulosa. At this time, which is about the eighth week, no differentiation is noticeable. But from the eighth week, the primordial ova begin to enlarge and multiply, the epithelium becomes more stable, and the connective tissue

stroma increases rapidly in amount. Next, the primordial ova sink into the stroma, infolding with them a layer of epithelial cells which form about each egg an epithelial tunic. Then the connective tissue becomes vascularized. Each ova and its tunic constitute a Graafian follicle. And finally, the large nucleus of the primordial ovum evolves into the germinal vesicle. (7)

During the development of the female genital glands, the ovary undergoes a frequent change of shape. It appears long, flat, bean-shaped, and oval respectively until it finally assumes its almond-shaped form. The size of the ovary increases, and the surface becomes smoother between birth and puberty. (7)

The ovary, like the testis, undergoes a migration, or descent. At about the third month of intrauterine development the ovary begins to descend from its original position into the pelvic cavity. The descent is probably forced by the unequalized traction exerted by the ovarian ligament when the Wolffian body and its connections to the ovary degenerate. The descent may also be aided by developing organs pushing downward. Like the morphological and physiological development, the descent to the ovarian fossa of Krause is not completed until puberty. (18)

A few days after the Wolffian bodies develop, (the 10 mm. stage) a groove develops in the thickened epithelium of the genital fold, in the region of the third thoracic segment.

This invagination deepens until the two lips at the caudal end fuse to form a tube, the important Müllerian duct. Minot believes that the Müllerian ducts are formed from the epithelium of the Wolffian bodies, but Arey, Bovée, Masson and Kaump, and others are firm in their belief that the genital fold forms the origin of the ducts of Müller. (3,7,40)

At first the Müllerian ducts are tubes fused caudally and open cranially as triangular areas. Soon the caudal end begins to grow downward, meets its fellow from the opposite side, and together they descend as the genital cord to the dorsal wall of the urogenital sinus. Meanwhile, the lips of the cranial extremity fuse into a funnel shaped tube which soon acquires denticulations that develop into the fimbria. (7,40)

Between the eighth and twelfth fetal weeks, the two adjacent ducts of Müller fuse. Masson and Kaump (40) and Bovée (7) advance the claim that fusion commences at the caudal ends, but Adair (1) and Arey (3) claim that their observations indicate that fusion starts between the middle and lower third of the ducts and progresses upward and downward from that point. According to Bovée, the process may be reversed in rare cases, and the fusion commence at the upper end, in the region that develops into the fundus of the uterus. Between the fourth and fifth fetal months, the process of fusion has been completed. At this time, the cranial ends of the Müllerian ducts are still separate tubes, the oviducts, while below, there is a single structure that is the

This invagination deepens until the two lips at the caudal end fuse to form a tube, the important Müllerian duct. Minot believes that the Müllerian ducts are formed from the epithelium of the Wolffian bodies, but Arey, Bovee, Masson and Kaump, and others are firm in their belief that the genital fold forms the origin of the ducts of Müller. (3,7,40)

At first the Müllerian ducts are tubes fused caudally and open cranially as triangular areas. Soon the caudal end begins to grow downward, meets its fellow from the opposite side, and together they descend as the genital cord to the dorsal wall of the urogenital sinus. Meanwhile, the lips of the cranial extremity fuse into a funnel shaped tube which soon acquires denticulations that develop into the fimbria. (7,40)

Between the eighth and twelfth fetal weeks, the two adjacent ducts of Müller fuse. Masson and Kaump (40) and Bovee (7) advance the claim that fusion commences at the caudal ends, but Adair (1) and Arey (3) claim that their observations indicate that fusion starts between the middle and lower third of the ducts and progresses upward and downward from that point. According to Bovee, the process may be reversed in rare cases, and the fusion commence at the upper end, in the region that develops into the fundus of the uterus. Between the fourth and fifth fetal months, the process of fusion has been completed. At this time, the cranial ends of the Müllerian ducts are still separate tubes, the oviducts, while below, there is a single structure that is the rudimentary uterus and vagina. Shortly after fusion of the lower portion is completed, the septum formed by the medial walls of the two ducts disintegrates leaving one chamber. During the fourth and fifth fetal months, there is an increase of tissue in the upper portion of the fused tubes which serves to differentiate the uterus from the vagina. Then during the sixth and seventh months of fetal development, the cervical portion of the uterus undergoes rapid growth, and becomes considerably larger than the body. During the remaining months until birth, cervical growth ceases, and the body of the uterus develops. However, the body does not attain the size of the cervix during intrauterine development. (7) The uterus continues to change size, shape, and position from birth until puberty. During the first four months after birth the uterus undergoes a marked decrease in size, losing nearly one-third of its natal length. From this period until approximately the sixth year there is little growth of the organ. But during the sixth year, or at the time of the second dentition the uterus experiences an increase in size of about twenty per cent. Most of this growth is confined to the body and the fundus. At the same time, the cervix begins to push into the vagina. Finally, after a second period of quiescence which lasts until just before puberty sets in, there is a general increase in the dimensions of the uterus during which the body and the fundus attain superiority of size over the cervix. Scammon avers that the second period

of post-natal growth is earlier and shorter than is usually recognized, however, he notes that the growth and time of this period are quite variable. Finally, the formation of the glandular tissue in the mucosa is completed and the organ has reached its final size, shape, and position with relation to the pelvic cavity and the vagina. (7, 50)

The origin and development of the vagina, the vulva, and the hymen are questions that have aroused considerable controversy, and as yet, no positive agreement has been reached.

It is rather generally accepted that at least the upper two-thirds of the vagina is derived from the caudal end of the fused Müllerian ducts. But there are three distinct schools of thought concerning the derivation of the external third. Several investigators believe that this lower third is also a product of the Müllerian ducts. Erna Vilas, 1932, A. K. Koff, 1933, Masson and Kaump, 1937, and others are of the opinion that the lower portion of the vagina is formed by an invagination of the uro-genital sinus toward the utero-vaginal canal. A third view, held by Bloomfield and Frazer 1927, and R. H. Hunter, 1930, is that the vulvo-vaginal chamber is derived from the mesonephric ducts. The origin of the lower portion of the vagina has an important bearing on the interpretation given to the hymen. (3)

In any case, there is a process of invagination, to a greater or lesser extent on the part of the urogenital sinus

during which that structure grows upward to meet the products of the Müllerian ducts which are descending.

Between the vagina and the vulva is the imperfect membrane known as the hymen. It is uncertain as to whether the hymen is derived from the vagina or whether it is a derivative of the vulva. Arey (3) accepts the belief that the vagina in its entirety is derived from the Müllerian ducts. He believes that the vagina pushes through the posterior wall of the urogenital sinus to complete the genital canal. As it pushes through, it forces the slight prominence (the _Müllerian tubercle)_ just below its point of entrance, into a transverse position across the sinus, and compresses it into a disk that becomes the hymen. According to this theory, the hymen is a product of the sinus and not of the vagina. However, we shall later see that the hymen has been found where no vagina is present. If, however, the sinus forms the lower one-third of the vagina, the hymen might well be present even though the vaginal portion derived from the Müllerian ducts were absent.

On the other hand, according to _Cunningham's Text-Book of Anatomy_, the hymen is formed from a slight fold at the tip of the vagina. Williams (_Text-book of Obstetrics_), also of the belief that the hymen is of vaginal origin, elaborates as follows: "In early embryos the hymen is composed of a solid mass of epithelial cells, and after proliferating rapidly for a time, those most centrally situated begin to

degenerate so that a lumen is produced."

An important substantiation for the theory that the hymen is derived from the vagina lies in the fact that there is a direct continuity between the upper surface of the hymen and the vaginal wall, and also there is a similarity in structure between the two organs. (6,13)

The clitoris is the atrophied remnant of the genital tubercle which was extruded at about the fifth fetal week. The embryonic genital folds evolve into the labia minora, and the genital swellings, which fuse in the male to form the scrotum, remain as separate ridges to form the labia majora. (34)

During the early development of the embryo, the caudal extremity of the gut terminates in the cloaca, a common vent into which open the allantoic, urinary, and genital ducts. The period when all of these tubes have the common opening is brief. Almost as soon as the connections are formed, the cloaca begins to divide into a dorsal rectum and ventral urogenital sinus. (3)

THE ANOMALIES OF THE FEMALE GENITALIA

There are innumerable ramifications of the various parts and organs of the reproductive system. However, the possible value to be attained by enumerating and describing each individual anamolous condition would not be commensurate with the energies expended in the task. For our purposes at least, it will suffice to outline the general types of deviations from the normal.

OVARIES

Commencing first with the genital glands, we find there exist five major types of ovarian abnormalities. These may be classified as follows:

1. Complete absence of the ovaries.
2. Existence of one or more small supernumerary ovaries.
3. Congenital atrophy or hypertrophy of the ovaries
4. Displacements of the ovaries.
5. Congenital cysts--especially dermoid cysts.

Complete absence of both ovaries is very rare. Morgagni, Pears, and Cripps all have reported cases of double absence.

Vidal and Chaussier have observed the absence of one ovary, while Thudichum has collected twenty-one such cases. However, West and de Sinéty both emphatically deny the plausibility of such a situation, believing that at least a vestigeal trace of the glands must be present. Bovée hesitates to deny completely that both ovaries can be absent, but casts grave doubt upon the possibility. He, too, believes that rudimentary evidence may be found, and supplements his claim by his observations on a supposed case of complete absence in which he discovered very small isolated patches of ovarian tissue scattered over the surface of the broad ligament. (7) Debierre admits the possibility of complete absence but states that such a condition must be accompanied by a decided arrest in development of the entire internal genital system. (16) However, on the basis of pure embryology this statement might not hold true, because the origin of the glands is considered distinct from the origin of the other internal organs. Debierre states that the ovaries are independent from the oviducts, uterus, and vagina, and that all the ducts may be absent without causing any variation in the structure or position of the ovaries. It has been claimed that the converse might be true. However, the recent investigations on sex hormones invalidates the latter assumption. According to the sex hormone theory, the ovaries secrete chemical substances which stimulate and regulate the development of the Müllerian duct derivatives and the associated sexual characteristics. Hence, ovarian maldevelopments necessitate defects of the other organs.

Closely related to absence of the ovaries is the rudimentary condition of these glands. Failure to complete development may affect the entire gland or only certain tissues. The most common condition in which parts of the ovary exhibit incomplete development is known as the primary cirrhotic ovary. Here, the connective tissue shows evidence of having undergone excessive growth, thereby inhibiting, or even completely preventing the development of the Graafian follicles.

At the opposite extreme from the absence of the ovaries we have the presence of supernumerary glands. Cases of this nature have been described by Beigel, Puech, Thudichum, Winckler, de Sinéty and others. (16) Bovée again casts doubt on the plausability of such a condition, claiming that the observers had probably mistaken the lobes of a lobulated ovary for extra glands.

Another problem is aroused concerning cases of atrophy of the ovaries. Debierre suggests that the type of congenital atrophy in which the ovules and ovisacs disappear similar to the degeneration following the menopause may merely be a type of rudimentary ovary. It is difficult to determine whether there has been a failure to develop or a degeneration. However, Rokitansky recognizes the possibility of prenatal atrophy on the belief that torsion or constriction of blood vessels to that organ may inhibit development. (7)

Cases of hypertrophy of the ovary are believed to

exist, but no recent literature on this condition was discovered.

Ovarian displacements are comparatively common in occurrence as well as widely varied in type and degree. It is natural to expect that any organ which undergoes an extensive migration, as does the ovary, might easily be deviated from its normal course as a result of the change in rate of development of an allied or surrounding organ, or by mechanical shock. These factors are used by Debierre to explain such anomalous descents as would lead the ovaries to Douglas's cul-de-sac (a pouch formed by the peritoneum of the posterior wall of the vagina and the anterior wall of the rectum), the inguinal canal, the obdurator foramen, the femoral region, and even into the labia majora. In the latter case, the descent of the ovaries parallels that of the testes, and the egg-producing glands come to lie in the female homologues of the scrotum. (16)

The inguinal hernia is the most common displacement, and usually affects both glands. The femoral type of hernia rarely affects both glands. In fact, Otte, 1857, published the only authenticated account of a double femoral displacement. Obdurator hernias, both single and double, have been observed by several investigators. (16)

Ovarian hernias are usually accompanied by maldevelopment of the other internal genitals. Rarely does the glandular displacement occur independent of other anomalous

conditions. Frequently the hernias of the ovaries are found in conjunction with displacement of the Fallopian tubes and the uterus, and very commonly the abnormal ovarian descent is complicated by an intestinal hernia. (16)

And finally, among the anomalous conditions of the ovaries, there are the cystic formations. A common form of congenital cyst affects the Graafian follicles through the failure of the ovarian epithelium to give rise to Pflüger's tubes which evolve into primary follicles and thence to Graafian follicles. Instead, irregular, epithelial-lined cavities are formed. Gradually the cavities increase in size due to the accumulation of the products of their secretion. The above explanation was developed independently by both Malassez and de Sinéty. (16)

Dermoid cysts are thick sacs containing such ectodermal derivatives as skin, hair, nails, teeth, sebaceous glands, and cerebral matter, as well as muscular tissue and dermoid tissues. In the more complex types, the cysts may contain organ-like masses composed of three germ layers. Misshapen representatives of all tissues and organs may be present. The exact cause of such phenomena is obscure, but several explanations have been advanced. One theory suggests that there has been an early arrest and isolation of misplaced blastomeres. Once enclosed in the ovarian tissue, these differentiated cell masses undergo a partial fulfillment of their primitive developmental potentialities. Kampmeier, 1929,

augmented the original hypothesis of Verneuil and Lannelongue to reach the above explanation.

A second theory, advanced by Loeb, 1915, and Brancha, 1926, explains dermoid cysts as the result of a partial parthenogenetic development of the ovarian eggs. Neither theory has any positive experimental proof. (3)

FALLOPIAN TUBES

Anomalies of the oviducts may be divided into the following categories: absence, rudimentary condition, multiplicity, displacement, and imperforation.

Debierre recognizes the absence of one or both oviducts independent of anomalies of the ovaries or derivatives of the Müllerian ducts. Bovée believes that complete absence of the oviducts must be accompanied by defects throughout the ducts of Müller. But Bovée admits that constrictions caused by adjacent parts may result in resorption of the Fallopian tubes or prevent their development. Such a condition would be independent of any maldevelopment of the Müllerian ducts.

Courty claims that the absence of the oviduct is very rare, and that even when the uterus is absent, the Fallopian tubes may be present. (7)

Bovée observed that where one of the Müllerian ducts has failed to develop, as in uterus unicornis, the oviduct on the defective side is completely absent. (7)

The rudimentary state of the oviducts is less commonly

found in the estimation of Debierre. His investigations revealed that unless mechanical constrictions inhibited maturation of those tubes, the incomplete development of the Fallopian tubes is only found accompanying serious uterine malformations. However, Bovée quotes von Winkel as having observed several cases in which there was considerable variation between the lengths of the two ducts, a fact that indicates a rudimentary condition in the lesser developed of the tubes. (7)

According to von Winkel, the oviducts may vary from 2 to 6 inches in length, but such variations from the normal length usually affect both tubes unless one is in the rudimentary condition. (7)

Olshausen (see 7) observed a modification of rudimentary oviducts in which the uterine ends of the tubes were well developed, but the fimbriae were absent from the glandular extremities, and the abdominal orifices were imperforate.

Although Debierre claims that multiplicity of the Fallopian tubes only affects an increase in the number of pavilions, Bovée quotes several authenticated cases of one or more complete supernumerary tubes. Most commonly, the supernumerary condition is characterized by a branching at the glandular end of one oviduct to produce two fimbriated extremities. Keppler (see 7) recorded a curious condition in which an extra pavilion, which had branched from one of the

oviducts, led to a third normally developed ovary. Less common is the condition in which there are multiple uterine orifices and branches which start directly from the uterus.

Displacements of the Fallopian tubes are quite frequent. Debierre contends that there is no interdependence between hernias of the ovaries and their ducts. However, such defects rarely, if ever, appear unless there is an accompanying malformation of the uterus or hernia of the ovary.

Like the ovaries, the Fallopian tubes may be misplaced into the inguinal canal or into the femoral region.

Obliteration of the lumen of the oviduct can be congenital, or pathologically acquired. The two types can usually be distinguished by the fact that congenital strictures generally affect the entire duct, whereas pathological closures are most frequently confined to a restricted portion of the tube. There is one exception to this generality; namely, that imperforation confined to the abdominal orifice of the fimbriated extremity may be a congenital stricture. (16)

Frequently the external appearance of the oviduct is normal in every way, but the lumen exhibits a marked decrease in diameter, closely approximating obliteration. (7)

UTERUS

Uterine anomalies constitute the most numerous and the greatest variety of types of genital abnormalities. The many possible developmental deviations that can occur during the fusing of the two ducts of Müller are directly accountable for the majority of the congenital defects of the uterus.

Following is a general classification of uterine abnormalities adapted and modified from that given by Bovée:

1. Complete absence of the entire uterus.
2. Rudimentary uterus.
    a. Hypoplastic uterus.
3. Absence of the cervix.
4. Rudimentary cervix.
5. Failure of two horns to develop and fuse.
    a. One-horned uterus.
    b. One-horned uterus with a rudimentary second horn.
    c. Two-horned uterus.
6. Incomplete fusion of the two uteri.
7. Persistence of the septum.
    a. In the corpus uteri.
    b. Throughout the entire length of the uterus.
8. Transverse partitions.
9. Imperforation and atresia of the uterus.

10. Atrophy and hypertrophy.
    - a. In the cervix.
    - b. In the corpus uteri.

11. Positional abnormalities.

It must be understood that the above classification of uterine anomalies is constructed for the purpose of facilitating description of the defects according to the anatomical divisions of the organ, but is inadequate in that it fails to indicate chronological relationships. In a subsequent section, another classification will be given which correlates the defects of the uterus from the point of view of their developmental interdependence.

The possibility of having complete absence of the uterus is another problem that divides students of the subject into two diametrically opposed camps. Bovée takes a most definite stand by claiming that "there is at least a trace of a uterus in every living female." He augments his statement with the contention that complete absence of the uterus occurs only in association with acephalia, acardiacus, or other cardiac anomalies which make extra-uterine life impossible. Bovée insists that the presence of some rudimentary uterine tissue must be present in every case of supposed absence of the uterus; consequently, he refutes the testimonies of Courty, Quain, and Steglehner who claim to have observed cases in which there were no internal genitals. In substantiation of this refutation, Bovée cites

the fact that he made supplementary examinations on a case of Künisch in which no internal organs of reproduction were observed, and that he found patches of rudimentary genital tissue that had been mistaken for enlarged lymphatic glands. Bovée has also found that careful histological examinations have proven the existence of very rudimentary bilobed or unfused uteri in cases that had been diagnosed as oviducts in the absence of a uterus. (7)

Debierre expresses an opinion similar to that of Bovée. However, for purposes of physiological study, he is less critical than the latter and regards cases in which the rudimentary condition of the uterus was so extreme as to reveal no immediate presence of that organ as cases of absence. With this broadening of the definition established, Debierre records several cases in which the uterus was ostensibly absent, but other internal organs were normal, even to the point where ovulation occured regularly. The last condition has been described by L. LeFort, S. Pozze, Munde, and Max Strauch. More frequently, cases of supposed uterine absence coincide with absence or atrophy of the vagina, oviducts, and ovaries. (16)

The rudimentary condition of the uterus ranges from a mere patch of uterine tissue or a slight thickening in the wall of the bladder as described by Veit (see 7), to an almost normal and functional organ.

There are many diversified modifications of the very

primitive state. The uterine tissue may be an undeveloped appendage to some other organ, or there may be a small solid cord connecting the two oviducts. Langenbeck (see 7) observed segregated patches of uterine tissue elements scattered over the surface of a rudimentary broad ligament.

Frequently, there are two separate solid cords connecting the Fallopian tubes and the vagina. Such a condition is termed a uterus bipartitus. A later stage finds the two cords fused, but still imperforate. Bovée asserts that some degree of imperforation usually exists in a rudimentary uterus.

The fetal or infantile uterus and the pubescent uterus are conditions in which the uterus has completed its embryonic development but has experienced an arrest in the maturation growth that normally occurs after the basic fusion of the two Müllerian ducts. The fetal type has the size and shape of the uterus as it appears at birth. The pubescent uterus results from an arrest in growth sometime between birth and puberty. Both the fetal and the pubescent uteri are accompanied by poorly developed external genital organs and aborted mammae as a general rule. However, the other internal genitals may appear quite normal. (16) Bovée includes the fetal and pubescent types of uterus under the term hypoplastic uterus. The general characteristics of the hypoplastic uterus are as follows: the organ is anvil-shaped, the cervix is larger than the body, and the latter is often bent over the former. The internal os is usually indistinct.(7)

Because of the nature of the process by which the two Müllerian ducts are fused, deviations from the normal affect the cervix and the body of the uterus differently. The lower portions of the Müllerian ducts usually tend to come together more readily than do the anterior ends; hence, two separate cervices occur less frequently than do two unfused bodies. However, the growth and development of the lower extremities of the ducts is often arrested so that the cervix of the uterus may be found absent or in a rudimentary state. In cases where the cervix is completely absent, the body of the uterus usually rests directly on the roof of the vagina, but rarely penetrates through to form a continuous canal.

In the rudimentary state, the cervix is characterized by being miniature in size, and having its lumen more or less completely obliterated. Imperforations occur at the internal and external orifice, one or both, and throughout the entire length of the cervical duct, but rarely, if ever, is a stricture localized at one point of the tube. (16) A common type of rudimentary cervix is a small pointed projection from the body having practically no lumen, and very minute orifices at either end. This is known as the conical cervix. (7)

The rudimentary cervix may merely rest on the vaginal roof without penetrating it, or it may enter the vagina like a fistula.

Very rarely, a double cervix is encountered. There are two modifications of this anomaly. In the majority of occurrences, the dividing septum projects downward from the body, but cases have been seen in which the septum continues upward from a persistent vaginal septum. (7)

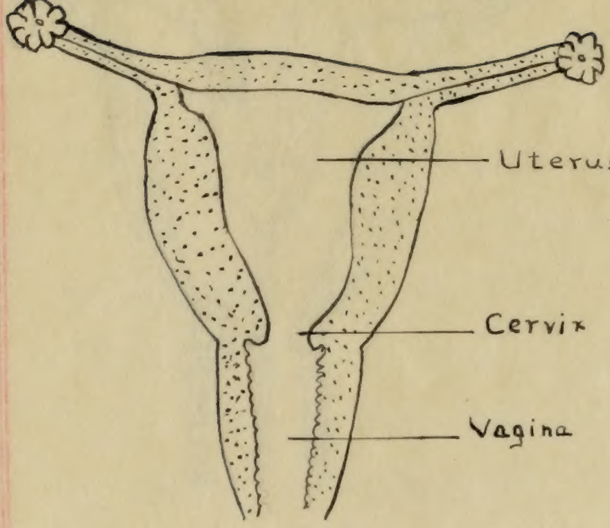
Bovée observes that a serious defect of the cervix rarely occurs without being accompanied by some anomaly of the body of the uterus.

Inasmuch as the body of the uterus is the first part of that organ to form from Müller's ducts, and inasmuch as the balance of opinion indicates that there is no such condition as complete absence of the uterus, it follows logically that absence of the corpus uteri is impossible. However, where the body does develop, it is subject to defects caused by the failure of one of its component elements to mature, or by the failure of the two basic ducts to unite. The first case of this nature is the uterus unicornis or one-horned uterus. This anomaly is the result of the failure of one of the ducts of Müller to develop; hence, the uterus is a unilateral organ. Usually accompanying this condition is a narrow vagina and a small cervix. The ovary and oviduct on the defective side may be absent or may exhibit abnormalities. The corpus curves upward and to one side from the cervix. It may be expected that all derivatives of the Müllerian ducts on the defective side will be absent. (7)

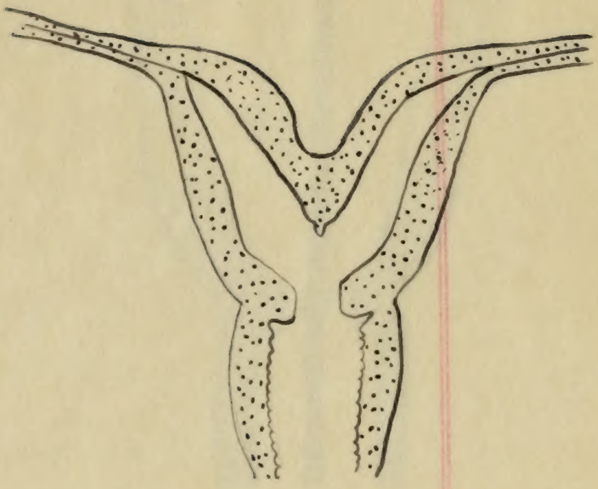
A slightly advanced version of the above condition presents a one-horned uterus with a rudimentary second horn--*uterus unicornis cum cornu rudimentario*. The rudimentary horn may appear in various states. It has frequently been observed as a thin, band-like strip of muscular tissue stretching between the oviduct and the other horn of the uterus. Generally, there is no continuous lumen connecting the oviduct, the rudimentary horn, and the normal horn. Bovée has found the rudimentary horn appearing externally as a small cylindrical cord, while the subserous portion was a rounded solid mass detached from the uterus and the ovary.

The oviduct connected to the rudimentary horn may be practically normal, or it may show the same developmental arrest that affected the uterus. But it can be expected that the cervix and the vaginal portion of the arrested duct of Müller will be absent when the horn is in a rudimentary state.

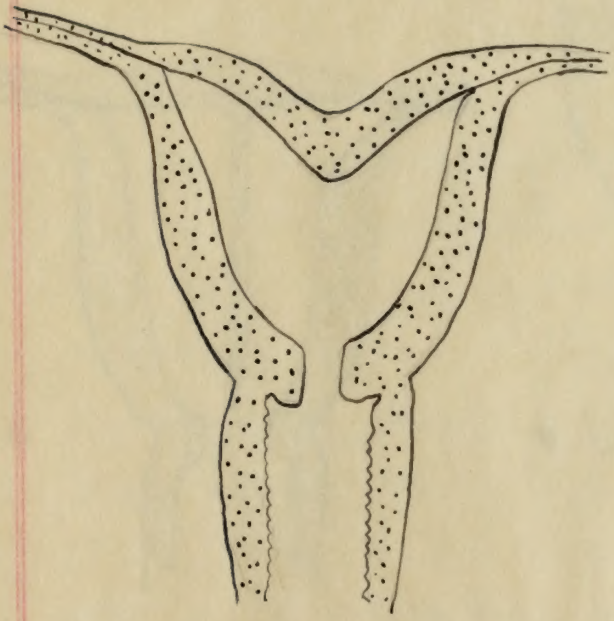
A final anomalous condition which may be said to affect the corpus uteri only is the *uterus bicornis* or *two-horned uterus*. The body of the uterus in such a condition consists of two divergent horns, both normally developed and both connected to a normal fused cervix. The left cornu is generally anteflexed, and frequently there is a band, the *vesico-rectal ligament*, which passes between the two horns from the rectum to the bladder. The cornua are seldom of ~~the~~ identical size. (16)


Uterus
Cervix
Vagina

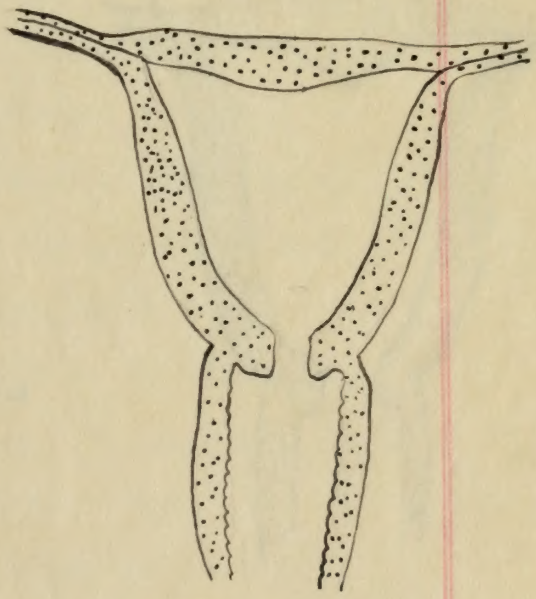
1.- Normal Uterus



2. - Uterus Bicornis



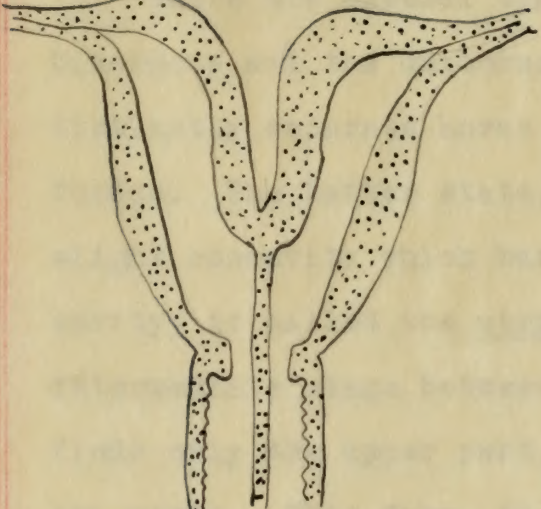
3. - Uterus Bicornis Unicollis



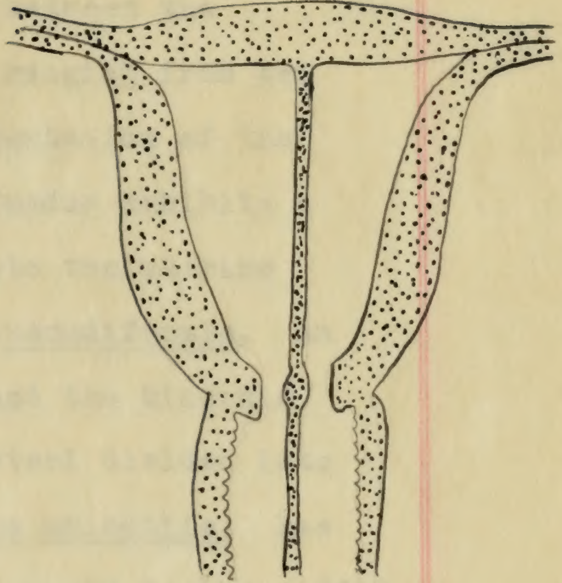
4.- Uterus Arcuatus

III a.

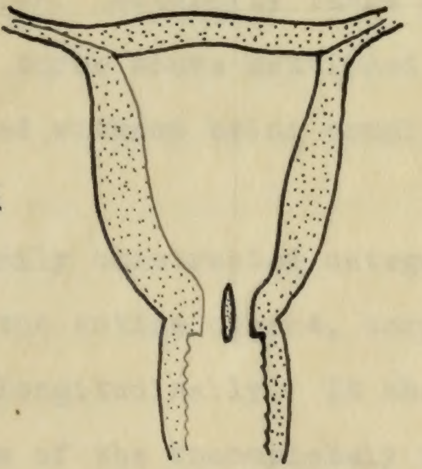
Fig. 1 - after Debierre.
Fig. 2, 3, 4 - adapted from Masson & Kaump.



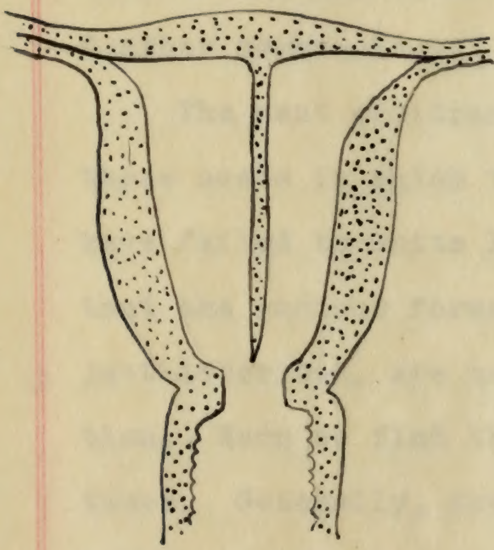
5. - Uterus Didelphys



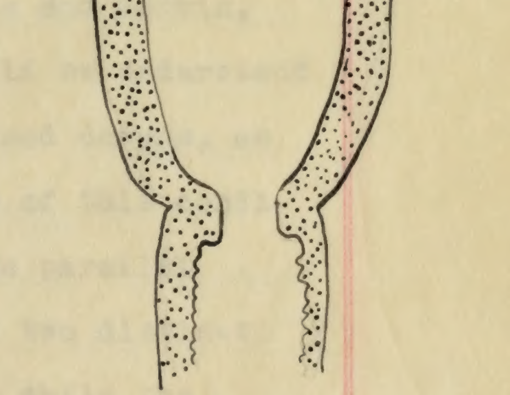
6. - Uterus Bilocularis, or Septus Duplex



9. Uterus-Biforis



7. - Uterus Bilocularis Unicollis



8. - Uterus Subseptus

III b.

Fig. 5-8 adapted from Masson & Kaump

There are several transitory stages between the bicornous and the unicornous conditions, ranging from two distinctly separate horns to a slight indentation of the fundus. The latter state, in which the fundus exhibits a slight concavity which barely projects into the uterine cavity, is called the uterus arcuatus or cordiformis. An intermediate stage between the arcuatus and the bicornis finds only the upper part of the corpus uteri divided into two parts. This form, the uterus bicornis unicollis, has two divergent cornua fusing at about what would be the middle of a normal corpus uteri. The fundus appears in the form of a rather deep depression. Naturally there are further subdivisions between the three above mentioned conditions, but they can be appreciated without being complicated by further terminology.

The next arbitrarily constructed category includes those cases in which the entire uterus, corpus and cervix, have failed to unite longitudinally. It should be understood that the various forms of the incompletely fused corpus, as just described, are merely less extreme cases of this condition. Here we find the uterus as two separate parallel tubes. Generally, the corpus is divided into two distinct cornua as in the extreme bicornous condition, while the cervices are enclosed in a common external sheath, but are separated internally by the medial walls of their original Mullerian ducts. This double uterus has been given the name

There are several transitory stages between the bicornous and the unicornous conditions, ranging from two distinctly separate horns to a slight indentation of the fundus. The latter state, in which the fundus exhibits a slight concavity which barely projects into the uterine cavity, is called the uterus arcuatus or uncudiformis. An intermediate stage between the arcuatus and the bicornis finds only the upper part of the corpus uteri divided into two parts. This form, the uterus bicornis unicollis, has two divergent cornua fusing at about what would be the middle of a normal corpus uteri. The fundus appears in the form of a rather deep depression. Naturally there are further subdivisions between the three above mentioned conditions, but they can be appreciated without being complicated by further terminology.

The next arbitrarily constructed category includes those cases in which the entire uterus, corpus and cervix, have failed to unite longitudinally. It should be understood that the various forms of the incompletely fused corpus, as just described, are merely less extreme cases of this condition. Here we find the uterus as two separate parallel tubes. Generally, the corpus is divided into two distinct cornua as in the extreme bicornous condition, while the cervices are enclosed in a common external sheath, but are separated internally by the medial walls of their ancestral Müllerian ducts. This double uterus has been given the name

uterus didelphys or uterus duplex. Frequently, the external peritoneum covering the two cervices may be absent. When this condition occurs, a portion of the bladder or the rectum may be found growing between the two independent uterine ducts. Each uterus commonly opens into its own vagina so that the genital canal is duplex right down to the vulva. However, double uteri have been observed opening into a common vagina. (7)

A rare anomalous variation of the uterus didelphys known as the uterus rudimentaris bipartis finds two separate uterine elements with their lumens completely obliterated. (7)

The next type of abnormality is one in which fusion has been completed, but in which the longitudinal septum has failed to degenerate, to a greater or lesser extent. As has been stated, when the two Müllerian ducts undergo fusion, their medial walls are joined together to form a septum, which in the normal course of events should disintegrate to leave a single uterine chamber.

Starting first with the most extreme condition of this nature there is the uterus bilocularis or uterus septus duplex. Here, the septum extends from the fundus throughout the length of the body and the cervix to the external orifice, and possibly also through the vagina to the hymenal ring. The external appearance of the uterus is normal, although Bovée asserts that the transverse diameter may be slightly increased. Also, according to this authority, both sides

of a bilocular uterus are rarely developed to the same degree. (7)

Generally the partition begins to degenerate at the lower extremity so that the cervical cavity will be single, while the corpus is divided into a double chamber. In a typical case of this type (known as uterus bilocularis unicollis or subseptus) the partition persists down as far as the internal orifice.

In the minimum state of septal persistence, the partition is in the form of a slight downward projection from the inner wall of the fundus. The terminology applied here is uterus bilocularis unicorporeus or uterus cordiformis.

Masson and Kaump (40) and Debierre (16) describe a rarer condition in which a remnant of the septum remains in the cervical region thus dividing the external opening into two orifices. The partition may also extend upward far enough to divide the entire cervix from the internal to the external orifice. A uterus with such a condition of septal persistence is known as the uterus biforis.

According to Bovée, the persistent septum is apt to be imperfect and contain perforations by which the two chambers communicate.

Breisky, P. Müller, Bidder, P. Budin, E. Blanc, and Trachet have observed cases in which there has been a transverse septum in the cervix uteri. This diaphragm-like abnormality consists of an evaginated fold of tissue from the

cervical wall. It may or may not have an aperture. Gueniot observed a case in which the transverse partition extended across the inferior part of the corpus, separating the body from the neck. (16)

Once again, it may be pointed out that an attempt to differentiate incompletely developed and atrophied forms of an organ presents difficulties. Most commonly, retrogression leaves the uterus in a state resembling a pubescent uterus. (16)

The uterus is commonly subject to various degrees of hypertrophy. There may be an excessive growth of the body, or the neck, or both. In cases of a hypertrophied cervix the corpus may exhibit inhibited growth and have infantile proportions. The enlarged neck may be elongated and cylindrical, or conical (due to an unproportional growth of the anterior lip.) The hypertrophied cervix can extend into the vagina, and may even pass through that organ and protrude from the vulva. (16)

Finally, there are positional abnormalities of the uterus which include anteversion, anteflexion, retroversion, retroflexion, and lateral versions and flexions to either side. Such anomalies may be due to differences in the degree of development of the products of the two Müllerian ducts, or they may be the result of unequal lengths in the various connecting ligaments. (16) Bovée also includes in his list of causes the possibility of atrophy of one side

of the organ, or of a ligament, and faulty attachment of the ligaments. (7)

The frequent occurrence of prolapsus of the uterus has been attributed to abnormal pressure as the result of excessive growth of some surrounding organ. (16)

VAGINA

The vagina is subject to defects similar to the preceding portions of the genital tract; namely, absence, rudimentary development, imperforation and atresia, division by partitions, both transverse and longitudinal, and abnormal external openings.

Though it is a rare occurrence, cases of complete absence of the vagina are recorded. However, inasmuch as the vagina is derived from two sources (the Müllerian ducts and the urogenital sinus) there may be absence of either the upper or lower portion. (16) Absence of the upper part of the vagina must be accompanied by some degree of arrested development in the other internal genitals that are derived from the ducts of Müller. (7)

In the rudimentary state the vagina may appear as a mere column of solid fibrous connective tissue. Another type of rudimentary vagina is one in which one Müllerian duct has failed to develop; hence, the vaginal passage is approximately halved in diameter and lies to one side of the median line. (7)

A third condition which may be considered rudimentary is where there has been a partial or complete failure of the upper and lower components of the vagina to integrate. The vagina is thus divided into two parts, the upper superimposed over the lower, and perhaps also separated from the inferior portion by a transverse membrane which represents the persistent roof of the urogenital sinus. (16)

Like the cervix uteri, of which the vagina is a continuation, the latter organ may be imperforate. The occlusion varies from total solidarity to the merest membranal stricture. (7)

The vagina may be divided by a longitudinal septum in a like manner to the uterus. Generally this partition is a continuation of the uterine septum, but Corazza observed a double vagina in the presence of a single uterus. (16) According to Remy (see 16) the above condition can be explained by the fact that fusion of the two Müllerian ducts begins at the middle of the genital cord; hence, fusion might proceed upward from this starting point, yet fail to progress caudally.

Bovée observes that this longitudinal septum may be cribriform, or may be entirely absent in places.

The transverse septa of the vagina resemble supernumerary hymens. These membranous strictures vary in number, and exhibit different forms and sizes of apertures that correspond to the types of hymeneal openings. However, the

transverse partitions may be devoid of any perforation. (16)

And finally, there are the abnormal openings of the vagina. The external orifice of the vagina has been found communicating with the rectum, the bladder, the urethra, and the abdominal cavity. These conditions may be the result of a developmental arrest during some transitory stage of the cloaca's existence, or they may be due to the fact that the vagina sought an alternative exit when the vulva failed to develop. (16)

HYMEN

Sources concerning the origin and certain anomalies of the hymen are largely composed of dogmatic antitheses. Few definite statements can be produced that have not been contradicted. And reasonable grounds can be found as substantiation for each view, because the paradoxical and irregular types of hymeneal anomalies defy any attempted explanation from any understood embryological process.

To review the situation briefly, one school of developmental anatomists believes that the hymen is derived from the inferior extremity of the vagina, while another asserts that it comes from the vulvar portion of the urogenital sinus. In support of the first view, it is cited that the epithelium of the upper surface of the hymen is continuous with, and of the same type as the vaginal epithelium. The supporters of the second theory attempt to transverse partitions may be devoid of any perforation. (16)

And finally, there are the abnormal openings of the vagina. The external orifice of the vagina has been found communicating with the rectum, the bladder, the urethra, and the abdominal cavity. These conditions may be the result of a developmental arrest during some transitory stage of the cloaca's existence, or they may be due to the fact that the vagina sought an alternative exit when the vulva failed to develop. (16)

HYMEN

Sources concerning the origin and certain anomalies of the hymen are largely composed of dogmatic antitheses. Few definite statements can be produced that have not been contradicted. And reasonable grounds can be found as substantiation for each view, because the paradoxical and irregular types of hymeneal anomalies defy any attempted explanation from any understood embryological process.

To review the situation briefly, one school of developmental anatomists believes that the hymen is derived from the inferior extremity of the vagina, while another asserts that it comes from the vulvar portion of the urogenital sinus. In support of the first view, it is cited that the epithelium of the upper surface of the hymen is continuous with, and of the same type as the vaginal epithelium. The supporters of the second theory attempt to substantiate their claim by pointing to the cases of S. Pozzi, Hofmann, Las Cassas de Santos, and others, in which there was absence of the vagina, yet, a somewhat normal hymen was present. (16) No conclusive information can be gleaned from a study of the relationship of the double hymen to the double vagina, because case observations yield evidence to support either view.

The abnormalities of the hymen may be discussed from the point of view of absence, number, structure, location, doubling, and shape, number and location of its perforations.

As in the question of the possibility of uterine absence, there is an affirmative and a negative opinion on absence of the hymen. L. Thoinot (55) states definitely, "Today the constant presence of the hymen is a dogma; every girl, every woman, always possesses either an intact hymen or the traces or debris of this membrane." However, the same author quotes F. Jayle as having found evidences of congenital absence. Bovée, usually a "neinsager" on questions of absences, basing his opinion on observations, and on the belief that the hymen is a derivative of the urogenital sinus, asserts that the membrane may be absent. (7) Debierre mentions that absence of the hymen is rare, but claims that it may be absent. (16)

Again there is a question concerning supernumerary hymens. From Debierre we learn that some students claim that the transverse membranous strictures of the vagina are extra hymens. However, such a view is held by a small

minority only, and the more general opinion holds that only one hymen is possible.

There are several structural anomalies of the hymen, some of which may be due to the persistence of the fetal or infantile form, and some, which are the result of an unproportional growth of certain component elements. (55) There are a group of abnormalities in which the membrane is particularly thick and fleshy with irregular and varied types of apertures that give the hymen the same appearance that it has in the infantile state. Among the names applied to these conditions are fluted hymen, tongue-shaped hymen, keel-shaped hymen, and fleshy hymen. Some hold the view that the thickened hymen is the result of hypertrophy. A final form in this group is the infundibuliform hymen, which retains its inverted position so as to resemble the calyx of a flower. (16)

The sclerosed, flaccid and vascular hymens are due to excess growth of one or more elements. The first type is rigid due to an overgrowth of fibrous and cartilagenous tissue. The second is very flexible because of the abnormal content of elastic fibers. And the vascular hymen is richly supplied with blood vessels to such a degree that a serious hemorrhage usually results from its rupture. (16)

The columnar hymen contains prominent parallel ridges over its upper surface. These seem to be a continuation of the ridges in the vagina.

An anomaly of hymeneal location that can also be described as a rudimentary condition concerns the depth of the hymen in from the vulvar opening. The hymen undergoes a migration-like movement outward from birth to pubescence. When the hymen is situated deeper in the vestibule of the vulva than is considered normal, it may be ascribed to an arrest in the descent of the membrane. (16)

A second abnormality of location finds the hymen elongated to form a valve-like extension covering the urethra, in such a way as to cause retention of urine.

An infrequent phenomenon is biforation of the hymen, or lateral doubling. So rare is its occurrence that many authorities doubt the possibility of its existence. Debierre claims to have seen a double hymen in conjunction with a double vagina. He believes that the condition is the normal accompaniment of an incompletely fused inferior portion of the Müllerian ducts. Bovée, although denying that the hymen originates from the vagina, agrees with Debierre that the hymeneal membrane will be doubled if a persistent vaginal septum remains in contact with the hymen. (7) Joseph Hyrtl opposes this view with his claim that the hymen is always absent when the vagina is double. (see 16) Debierre avers that his personal observations indicate that Hyrtl's statement needs modification; that absence of the membrane often accompanies a double vagina, but there is an equal possibility that the hymen may be present in the double form. (16)

Anomalies of the aperture of the hymen are not so subject to controversial views as are the other defects, because a disagreement over characteristics of an existent type is easily settled by the formation of an additional category.

Generally, the abnormalities of the hymeneal aperture are merely different degrees or modifications of the semilunar, annular, or linear types already described. There are also apertures that appear as intermediate forms between the normal types, or combinations of the characteristics of two or three of the common forms. A rare defect, not closely allied to the normal apertures is the fimbriated hymen. The edges of the opening are markedly denticulated, giving a fringed appearance. (16)

The cribriform hymen is an anomalous form of the membrane in which there are several small orifices instead of one main opening. (16)

A double aperture in the hymen has been discussed with relation to a doubling of the membrane to correspond with a septate vagina. The dual openings may occur independent of this condition, in which case it appears as though a membranous tongue passes through the aperture, dividing it. The partition has been observed running longitudinally and laterally. (6, 16)

Finally there is the condition known as the imperforate hymen. The opening may be entirely absent, or so minute

as to be the equivalent, for physiological purposes. The failure of the central cells to degenerate and produce an aperture obviously is a serious anomaly from the physiological standpoint. (6, 7)

EXTERNAL GENITALS

The external organs of generation are derived from a different source from the internal parts; hence, they are generally independent of the defects of the Müllerian ducts. However, due probably to the effects of a sex hormone, serious abnormalities of the ovaries or the genital canal may result in the arrested development or absence of one or several of the external parts. (7)

Occasionally the genital furrow fails to invaginate causing an absence or major atresia of the vulva. (16) Persistence of the cloaca also precludes any presence of a vulva. Absence of the vulva does not always prevent the vagina and the urethra from finding communication to the exterior. These ducts may open directly to the surface in the vulvar region, or they may join the rectum in a similar fashion to their more primitive cloacal fusion. (16)

There are two types of hypospadias recognized in females. In one, the perineum completes its formation, but the urogenital sinus retains its embryonic state as a long narrow passage into which the vagina and urethra enter. The second type lacks a urethral canal; hence, the vagina and the neck

of the bladder open together directly into the vestibule. (16) Hypospadias is usually accompanied by hypertrophy of the clitoris.

Epispadias is a rarer condition. It is usually accompanied by multiple defects of the bladder, anus and other surrounding organs. Debierre believes it to be due to an imperfect disposition of the allantois, causing interference with the proper development of all the lower organs of the urogenital system. Instead of a vestibule and a urethral meatus, there is a shallow groove. The clitoris is usually bifurcated in an epispadias, and each labium minor is united to one half of the clitoris. (16)

The labia majora and labia minora have both been found absent. S. Pozzi described a case in which there were no labia majora, but the inner lips were present. The labia minora only, have also been absent according to Hotman, de Villiers, Percheaux and others. (16) The arrest or limited development of the genital folds and the genital swellings is usually coincident with a malformation of the urogenital sinus and a general underdevelopment of the entire genital system, internal and external. (16)

Fusion between the various elements of the labia majora and minora has been known to occur. The large and small lip of each side may fuse to produce a single pair of lips. Also, and more serious physiologically, the two labia minora may fuse, as may the labia majora, thus causing an occlusion

of the vulva. (16)

Hypertrophy may affect either pair of labia to produce an enlargement of the lips. Extreme hypertrophy of the labia minora seems to be an inherited characteristic in the Hottentot women. In many cases the inner lips protrude from the vulva as far down as the knees. Other negroid tribes show a similar inheritance of hypertrophied labia majora, although the outer lips have never been found approximating the size of the labia minora of the Hottentot women. (16)

And finally, there are the anomalous conditions of the clitoris. Complete absence of the clitoris is not a proven phenomenon, because extreme epispadias may cause such a bifurcation that the erectile organ cannot be recognized. However, investigators have claimed the organ to be absent in such conditions.

Frequently, when the vulva is developmentally defective, the clitoris is but a slight rudimentary projection, similar to its embryonic ancestor, the genital tubercle.

The clitoris is frequently subject to the form of giganticism termed hypertrophy. When in this state, the clitoris has been known to expand to several times its normal size, even exceeding the dimensions of the erected male copulatory organ. (16)

HERMAPHRODITISM

The anatomical description of the innumerable forms and modifications of hermaphroditism is a gigantic task within itself. Countless accounts and records of monsters exhibiting some degree of structural bisexuality have accumulated since the time when men first began to take intelligent notice of deviations from the normal. For our purposes, several basic definitions and a general description of the nature of hermaphroditism must suffice.

Hermaphroditism is the condition in which one individual possesses the reproductive organs of both sexes, and can produce ova and sperm. In the ideal state, the hermaphrodite is physiologically as well as morphologically bisexual. No authenicated case of a functionally hermaphroditic human being is known.

Human hermaphrodites are divided into two main types. First, there is the true hermaphrodite in which there is histological evidence of both ovarian and testicular tissue. The second type, the false hermaphrodite, has the glands of one sex only, but has other organs of both sexes. (16) For practical study there is no great distinction between the two types, because the so-called true hermaphrodite has only one pair of its glands functional, thus making it physiologically similar to the false type.

There is a further subdivision of hermaphroditic types

that is usually applied with special reference to the true form, but can pertain as well to false hermaphrodites. These types are gynandry and androgyny. The former refers to those hermaphrodites who, on the basis of glandular function, are fundamentally female, and the latter type refers to those who are basically male by the same criterion. (16)

This being a study of the teratology of the female genitals, attention will therefore be restricted to gynandry.

Typically, the gynandrist has ovaries and the products of the Müllerian ducts. But externally, the appearance is masculinized by the fusion of the labia minora and majora and the hypertrophy of the clitoris, and frequently an excess hirsute growth on the face, chest, and lower abdomen. Most often, there are accompanying anomalies of the internal genitals. As can be appreciated, there may exist endless modifications and degrees of masculinity. The vagina and urethra may even communicate to the exterior through the hypertrophied clitoris, but usually their external opening is at the base of that organ. So complete have been some cases of gynandry that one (rarely both) ovary has descended into the fused labia majora to assume the position of a testicle. (16)

Once again let it be noted that the account of the multiple ramifications of hermaphroditism, as well as the other genital anomalies are herein being subordinated to a survey of the interrelating factors suggested as causes of these malformations.

THE EMBRYOLOGY
OF GENITAL ANOMALIES

Recently, strong emphasis has been placed on the endocrines as a causative factor of genital abnormalities. In order to understand properly, and to evaluate this source of the defects, the time of the appearance of each type of malformation must be known. Therefore, the following outline of the chronology of the anomalous conditions is given.

By way of review, we shall resort to Fürst's five stages of development of the genitalia. (see 7)

1. From impregnation to the fifth fetal week, the genital fold forms, and gives rise to undifferentiated glands and tubes. Differentiation starts after the fifth week.

2. During the eighth to the twelfth week of fetal life, the Müllerian ducts undergo their fusion. The difference between the corpus and cervix uteri becomes recognized. At this stage the cloaca divides into the anal and urogenital openings.

3. From the twelfth to the twentieth week, there is fusion of the cornua and the depression of the fundus disappears. The external orifice of the uterus develops and the vagina becomes distinguishable. The sexual tubercle atrophies into the clitoris, and the sexual folds and swellings

develop into the labia minora and majora, respectively. The hymen is formed at about this same time.

4. The fourth stage extends from the twentieth week of intrauterine existence to birth. It is a period of maturation of the vagina and growth of the uterus.

5. And finally, there is the period from birth to puberty during which the uterus and the external genitals mature and grow to their final form and dimensions.

If there is an arrest in the development of the entire genital ridge during the first five weeks after fertilization, both the ovaries and the Müllerian ducts will be absent, or in a very rudimentary state. Localized arrest of the ridge will affect only one of the above parts, and may permit the other to continue its development.

The various forms of the incomplete fusion of the two Müllerian ducts originate from the eighth to the twentieth week. Complete doubling of the uterus and vagina indicate a disturbance before the twelfth week. Also, a failure of the products of one of the Müllerian ducts to develop beyond the rudimentary state usually has its cause during the first dozen weeks.

The bicornous uterus and its modifications can be traced to an arrest during the early part of Fürst's third stage. Also, in this period there arise the disturbances which prevent the septal degeneration, and which cause defects in the external genitals.

Inhibitions during the fourth and fifth stages give rise primarily to such anomalies as the infantile and the pubescent uterus.

Masson and Kaump include a list of factors that have been suggested as immediate developmental causes of uterine malformations.

1. Many writers are of the opinion that some form of cloacal persistence with possible coincidental intestinal anomalies give rise to defects of the uterus.

2. Anomalies of the trunk or pelvis, and of the organs therein contained constitute another widely suggested cause. R. Meyer and Kussmaul advance a variant of this theory which attributes uterine anomalies to the faulty development of the ligaments adjacent or connected to it, which result in torsions or unequalized traction.

3. The presence of tumorous growths between the Müllerian ducts has been considered as a factor preventing their complete and normal fusion.

4. A very generalized statement of cause attributes the uterine defects to developmental failures, resulting in the abnormal fusion of the Müllerian ducts, or failure of the longitudinal septum to disappear.

C. W. Anderson, 1931, developed a theory based on the rate of fusion of the Müllerian ducts. According to his hypothesis, premature fusion produces a solid rudimentary uterus, and absence of the vagina. Delayed fusion results in

a unicornous uterus with one rudimentary horn. The bicornous uterus with either single or double cervix is due to partial fusion. Complete failure to fuse causes a doubling of the uterus. (40)

The above factors are based on developmental failures, which in turn are caused by one or more basic conditions to be discussed later.

Following is a table in which the malformations of the products of the Müllerian ducts are arranged in the approximate order of the time of their development.

1. During the first five weeks.
    a. Absence or extreme rudimentary condition of the oviducts, uterus, and vagina.
    b. Unilateral rudimentary conditions.
    c. Obliteration of the lumens.
    d. Multiple pavilions of the oviducts.
2. Eighth to twelfth weeks.
    a. Unilateral rudimentary conditions.
    b. Double cervix (uterus didelphys).
    c. Double vagina.
3. Twelfth to twentieth weeks.
    a. Uterus bicornis.
    b. Uterus bicornis unicollis.
    c. Uterus arcuatus.
    d. Uterus bilocularis.

   - e. Uterus bilocularis unicollis.
   - f. Uterus subseptus.
   - g. Uterus biforis.
4. Twentieth week to birth.
   - a. Infantile uterus.
   - b. Atrophies.
   - c. Hypertrophies.
5. Birth to puberty.
   - a. Pubescent uterus.
   - b. Atrophies.
   - c. Hypertrophies.

Thus, it can be seen that there is a rather definite uniformity and logical sequence to the formation of the abnormalities of the reproductive organs.

CAUSATIVE FACTORS
OF GENITAL ANOMALIES

The list of factors that have been suggested to account for the presence of anatomical malformations is almost endless, embracing, as it does, nearly the entire gamut of natural and man-made phenomena. Barometric pressure changes, X-rays, climatic conditions, galvanic action, chemical substances, mechanical and psychological shock, age and compatability of parents, and nearly everything from witchcraft to the ultra-scientific have been offered as possible causes.

The causative factors considered in this paper are restricted to those that have some factual basis from concrete scientific evidence, or that are plausible, generally recognized theories.

Attempted explanations for the formation of genital abnormalities are advanced from three aspects; the genetic, the developmental rate, and the endocrinological.

Commencing first with the genetic factor as a cause, we find briefly, that evidence leads to the belief that there are special chromosomes which seem to have a sex-determining function. In Man, there are two types of sex chromosomes, an X- and a Y-type. The presence of a pair of X-chromosomes in one zygote indicates that the fertilized egg has the potentiality to develop into a female. If one X-

and one Y-chromosome are present in the zygote, a male individual will be produced. Going back further into gametogenesis, it is noted that the primitive female germ cell contains two sex chromosomes. During the reduction division in which the haploid number is produced, each cell half receives one of these sex chromosomes. The spermatogonia, on the other hand, have two types of sex chromosomes, consequently, during their reduction division two different types of individuals are produced: one which contains an X-chromosome, and one which contains a Y-chromosome. Thus, if a spermatozoön of the first type fertilizes a mature ovum, the zygote will receive a pair of X-chromosomes, and produce a female. If the second type of sperm cell acts as the fertilizing agent, the zygote will have both the X- and the Y-chromosomes, and produce a male. (62)

Basically, the Gene Theory claims that each chromosome consists of a string of genes. Each gene is considered to be of a special chemical composition, and it may also elaborate chemical substances. Individual characteristics are the resultants of the reactions between the chemicals of two or more genes. (11)

However, not only are the genes responsible for the morphological and physiological characteristics of cells, tissues, organs, and organisms, but it is also believed that there are certain genes whose function is to regulate the time and rate of development of the various organic parts. The theory of the presence of the rate genes plays an

important part in the interpretation of the causes of genital anomalies. (51)

Thus, the presence of a pair of X-type sex chromosomes in a zygote merely indicates that it has the potentiality to produce a female. Unless there is a harmonious interaction of the rate genes, the normal processes cannot proceed.

Crew adds another factor which he calls the minimum stimulus stage. According to his theory, each tissue experiences a critical period during which time it is sensitive to the stimulating effect of the gene or genes which cause its differentiation or growth. More specifically, the basic genetic constitution of an organism may be feminine. This means that the undifferentiated gonad has the potentiality to develop into an ovary. However, unless the female-determining gene-complex elaborates its stimulating substance at a precise stage--the period of the minimum stimulus--the gonad will not continue its development into an ovary. (11)

As fetal life advances, the processes of stimulation become more complicated, and more dependent upon the proper development and function of more organs.

Another possible factor of importance in explaining developmental abnormalities of the reproductive organs lies in the displacement of genes. It is believed that during the complicated cell divisions, parts of the chromosomes may be become broken off, thereby losing their proper location or being entirely lost. Should such phenomena occur, it

follows that the portion or process for which the displaced genes were responsible would fail to materialize. (11)

Considerably more attention has been given the role of genetics in relation to hermaphrodite formation. Inasmuch as the greater part of this work has been done on insects, much information concerning the origin of anatomically bisexual human beings is a reinterpretation of the entomological findings in terms of the human's genetic make-up. In order to draw such inferences, it is necessary to assume that human hermaphroditism and gynandromorphism are essentially synonymous. Actually, the former term applies to animals containing a mixture of the sexual organs of both sexes, whereas gyandromorphism refers to a mosaic mixture of the tissues of both sexes. However, inasmuchas the human hermaphrodite does not exhibit functional bisexuality, his anomalous condition is the equivalent of the mixed sexual tissues of the gynandromorph.

T. H. Morgan advanced the Somatic Segregation Theory to explain the formation of hermaphrodites. According to this view, at some critical cell division stage a separation of chromosomes occurs in such a manner, that both an egg-producing and a sperm-producing organ are formed. In a very simplified practical application, this means that the primitive cells destined to form the gonads undergo an accident during some cell division whereby one or more of the

cells loses one of its sex chromosomes. The cell so affected will give rise to testicular tissue, while the normal cells will produce ovaries. To reach such a conclusion, Morgan assumes that each individual cell and tissue will develop according to its chromosomal constitution. Thus, if primitive tissue with the paired sex chromomes indicating a female-producing potentiality should lose one of its chromosomes, it would have the genetic make-up of male-producing tissue, and, according to Morgan's theory, develop as male tissue, independent of its sexual incongruity with its surroundings. (43)

This theory is designed to explain only such forms of hermaphroditism as contain the glandular tissue of both sexes. It does not account for the types which are glandularly unisexual, but have the other sex organs mixed.

Crew utilizes and augments this theory to account for the occasional cases of hermaphroditism in birds. He states, "If in a group undoubted, and otherwise inexplicable, cases of gynandromorphism are found, then in that group the internal secretions of the gonads do not constitute the sole controlling forces in sexual differentiation and the cells of different parts can pursue their differentiation under the direction of their own genotype."

When applied to human beings, this theory of hermaphrodite formation is also based on the fact that the loss of one sex chromosome from a female zygote or embryo leaves the resultant cells to develop as male tissue. Or to explain

the theory in Crew's own word, "In a female zygote, one X-chromosome was eliminated at the first cleavage division of the fertilized egg, or according to the grade of maleness in the characterization, later at some division of a cell in those areas which are to be involved in the sexual characterization." (11)

Crew's elaboration on the view expressed by Morgan makes the theory more inclusive, and permits it to embrace forms of hermaphroditism in which there is only one type of glandular tissue.

However, both Morgan and Crew developed their theories prior to Painter's discovery of the presence of the Y-chromosome in the human male. In the light of this more recent finding it would seem that the above theories are invalidated, because, for the genetic constitution of a tissue to change from female to male, not only must it lose one of its X-chromosomes, but in addition, it must acquire a Y-chromosome.

Another genetic interpretation of hermaphroditism is found in the Balance Theory of Intersexuality. This theory is based on the fact that normal development depends on a definite ratio between the sex chromosomes and the autosomes, and also between the sex genes. A relative excess of one type of gene over another may alter the final outcome. The greater the disturbance of balance, the more pronounced will be the expression of hermaphroditism, and the earlier the change will be produced. (51)

Bridges (57) illustrates the mechanism of the Balance Theory in producing gynandromorphs in Drosophila as follows:

The normal female has a ratio of one sex chromosome to one autosome. (IX : 1A).

The normal male has a ratio of one sex chromosome to two autosomes. (1X : 2A) Therefore,

3X : 2A is the ratio for a super-female.

1X : 3A is the ratio for a super-male.

2X : 3A is the ratio for an intersex. (51)

Crew criticizes the use of the Balance Theory as pertains to the explanation of human malformations on the grounds that it implies the existence of polyploidy.

As a final explanation of hermaphroditism based purely on genetics, there is the theory suggesting the possible existence of a gene or genes for intersexuality. Crew defined these as a certain organization of chromatin material in a particular area of a particular chromosome, that differs from that arrangement of chromatin in the same location that is associated with the development of normal sexual characteristics. This disarrangement of chromatin produces a disturbance in the internal environment such that the normal properties of femaleness are altered in the direction of maleness. Such a theory not only involves the genital tissues, but also takes into account the influence of the endocrines. (11)

Crew prefers the above theory to the Balance Theory,

on the basis that a disruption in the composition of the chromosomes is more plausible, and more apt to occur, than is a disturbance (through loss or multiplying) in the distribution of the chromsomes.

R. Goldschmidt and his associates, 1923, concluded from their experiments on cross-breeding insects that one race may have genes with a stronger sex determining potentiality than others. Thus, unless the female-determining power of the Y-chromosome and the male-determining power of the X-chromosome are balanced, an intersex will be produced. When the male-determining power is stronger, either a super-male or a female with male tendencies will be produced, and vice versa. (60)

Crew criticized the application of Goldschmidt's theory of intersex formation to Man on the grounds that human beings do not possess a Y-chromosome. However, since Painter established that both sexes of human beings have 48 chromosomes, and that the male has both an X- and a Y-chromosome, Crew's objection is invalidated. (62)

Allen avers that the majority, if not all cases of hermaphroditism in Man are found in offspring of pure white races, and not the product of mixed races. This observation is considered an important piece of evidence preventing the application of Goldschmidt's theory to explain human hermaphrodites. (56)

It is obvious that if genetics is a positive factor in

causing anomalies, the defects should be hereditary. As yet, there is too great a paucity of statistical evidence and case histories to make definite conclusions possible. However, the information that is available tends toward a positive indication.

Murphy studied the occurrence of genital malformations from the point of view of heredity, and concluded that abnormalities occur most frequently in families that have a past history of having produced defective offspring. (44)

Macklin's observations on twins (monovular and binovular) with relation to the inheritance of anomalies, led her to the belief that inherent defects in the determiners for development are responsible for the great majority of congenital malformations. (37)

Rupilius, Broster, and Apert who have been active in the study of hermaphrodite formation, are of the belief that heredity plays a role in the development of this condition. (31) O'Farrell has recently concluded observations which make him of the same opinion. (46)

Far from the majority of malformations have been observed to be hereditary. Nor does the same defect appear heritable in all cases. The lack of uniformity of inheritance of anomalies, as may be inferred from available evidence, indicates that genetics is but one of a group of factors that cause genital malformations.

The work of Stockard (53) concerning developmental rates during embryonic processes, forms an important aspect in the explanation of genital anomalies. As a result of his researches on the fish Fundulus, Stockard discovered that an artificially induced retardation of embryonic development definitely causes a structural deformity. If the inhibiting influence is exerted early in embryonic life, there will be a gross malformation affecting the entire body. If the retardation occurs later, the defect will be more localized.

Stockard observed that there are several "indifferent" periods in embryonic development, when cell division and growth occur slowly, and at a fairly uniform rate throughout the organism. Retardation has no deforming effect during such periods. But there are other critical periods during which cell division is generally speeded up, or when a particular locality exhibits extreme activity in proliferating or budding for the formation of an organ. Retardation during such periods causes deformities, rudimentary conditions, and possibly even absences of organs.

These phenomena are explained by the fact that each organ is derived not only from a definitely located primordium, but must also be derived during a limited moment of development. (53) At, and only at this critical moment, the internal environment of the embryo is favorable for a particular process of growth and development. When retardation occurs, the rates of all parts are reduced to

equality. However, when the inhibiting influence is removed, the differential rates are not reestablished with sufficient promptness. The internal environment changes before the proper rates are resumed, and the organ undergoing its crucial initial stages of development loses the necessary stimulating conditions and therefore produces a stunted or defective product. (53)

Stockard, and Lewis, 1909, have both affected retardation by lowering the temperature, by mechanical shock, and by chemical means. The latter inhibiting factor and possibly one or both of the others, may be used to explain human deformities, because several of the chemical effecters are transmittable from mother to fetus via the blood stream. (53)

Stockard concluded his research with the definite claim that all non-hereditary malformations must be due to a retardation of the rate of development. Perhaps this statement is too inclusive. Granted, his experimental evidence indicates that retardation of growth can account for structural abnormalities from such a gross type as double monsters to very minor defects of localized organs and tissue. But, there is no evidence or inference that developmental rate is a causative factor in the formation of hermaphroditic individuals, unless, of course, he regards hermaphroditism as a hereditary defect caused by retardation through the rate genes.

Crew, in connection with his discussion of the minimum stimulus stage, offers a suggestion which might partially

explain hermaphroditism, in a limited form, in terms of developmental arrest. According to Crew's view, once the gonads become differentiated they secrete sex hormones which direct the development of the other organs of reproduction, in such a way that an ovarian secretion will cause the Müllerian ducts to flourish, and the Wolffian derivatives to cease development, and the converse processes for a testicular secretion. Thus, should retardation occur in such a manner as to inhibit the sex glands, and prevent the secretion of the hormones, both the Müllerian and the Wolffian ducts would develop together and ultimately yield organs of both sexes. (11)

But Crew's argument accounts only for hermaphrodites having the ducts and external organs mixed. Stockard's theory still fails to account for the occurrence of true hermaphrodites that contain both ovarian and testicular tissue.

It must be noted that Stockard's conclusions have been proven on the fish Fundulus only. Application of his principles to explain anomalies in Man are hypothetical, and are not based on experimental evidence.

And final in the list of suggested causes of genital defects is the endocrine factor. Although considerable study has been devoted to the structure and function of the glands within recent years, this field is so extensive

that knowledge concerning it is still quite elementary and limited. The realization of this fact is strongly impressed on one who attempts to determine which gland or multiglandular syndrome forms a basic causative factor of genital abnormalities.

The ovaries are themselves glands, and, as shown by recent investigations, they secrete hormones which stimulate the development and function of the genital canal and the accessory organs of reproduction.

There has been considerable question concerning the presence of sex hormones. Kellog, 1904, Prell, 1915, Kopec, 1912 and 1922, Meisenheimer, 1909, and Hegner, 1914, and others have transplanted gonadal tissue in insects without creating any change of sexual characteristics. From these experiments it was concluded that there are no sex hormones or regulating secretions from the gonads. However, these results are now known to apply to insects only, but have no relation to the sex physiology of Man.

Recently it has been rather conclusively demonstrated that the ovaries secrete one or more sex hormones. Several compounds have been extracted, all of which are chemically similar. (58) According to Evans, the three foremost compounds, oestrone, oestriol, and oestradiol, probably differ in degree of purity and hydration only. He notes that oestriol is one-half as potent as oestrone, whereas oestradiol is two to four times more active chemically.

It is fairly well established that the female sex hormone (or hormones) is secreted by the ovaries, and probably by the corpora lutea and parts of the genital ducts. (56, 58, 59)

Allen claims that the embryonic gonad is stimulated to elaborate the proper sex hormone by the genetic make-up, and by gonadotropic hormones from the anterior pituitary. According to Allen, the cortex of the gonad elaborates the female determining substance, and the medulla produces the male sex hormone. (56)

The sex hormones serve to direct the development of the appropriate organs of generation, as well as to cause the development of the proper secondary sexual characteristics. (56)

Obviously, should the ovary fail to elaborate its hormone at the proper rate, corresponding anomalies of the related organs will result.

However, the ovarian function is not an independent phenomenon. There is a marked interrelation between the gonads, the pituitary and the adrenal glands.

According to current belief, the basophilic cells of the anterior lobe of the pituitary gland elaborate two physiologically different gonadotropic substances. Zondek termed these hormones Prolan A and Prolan B. The first is a water-soluble agent which has a follicle-stimulating effect. Prolan B, the non-water-soluble fraction is a luteinizing

hormone. These pituitary principles stimulate the development of the gonads to mature ovaries, direct the formation of the corpora lutea, and the concomitant production of oestradiol. (58, 59)

The ovarian secretion, on the other hand, exhibits a reciprocal effect, in that excess oestradiol inhibits the function of the pituitary. (58)

Hyperfunction of the adrenal cortex is also believed to affect the gonads, either directly, or through a pituitary-adrenal syndrome. In general, it has been noted that a hyperfunction of the adrenal cortex (usually, but not always indicated by a cortical carcinoma) is accompanied by a depression of the ovarian function, and the development of masculine tendencies. (58)

Grollman is of the opinion that the adrenal cortex has no effect on the gonads. He offers the hypothesis that there exists transient androgenic tissue between the cortex and the medulla which exerts an influence on the gonads similar to that influence attributed to the cortex. (61)

There is also an interaction between the pituitary and the adrenal glands. Present evidence reveals that the pituitary elaborates an adrenotropic principle which seems to stimulate the adrenal cortex. Evans, 1932, demonstrated that hypophysectomy results in an atrophy of the adrenal cortex which can be repaired and prevented by the administration of certain pituitary extracts. (58, 59) Similarly, that

condition of the adrenal commonly considered as cortical hyperactivity produces changes in the pituitary, most noteworthy of which is the decrease in the proportion of the basophilic cells. (61)

The thyroid gland has also been found to exhibit abnormalities in several cases of defective genital development. At present, the concrete knowledge concerning the role of this gland in relation to anomalies of the reproductive organs is largely limited to the fact that thyroidectomy in young children results in some degree of sexual infantilism. (58)

It is evident that there is insufficient information on which to base any definite claim as to the basic causative gland in the chain of malfunctions. In any case, the gonads seem to be affected ultimately in such a manner as to disturb their hormone secretions, which, in turn, produces malformations of the related genital organs.

Research on the glandular causes of hermaphroditism has received considerably more attention than has been given to the general genital anomalies; hence, there is far more information relating to the effect of the individual glands.

In 1910 E. Apert (see 31) noted that hermaphrodites who were basically female also exhibited a tumor of the adrenal cortex. This finding stimulated research on the adrenals. Apert concluded that the cortico-adrenal carcinoma caused hermaphroditism. He believed that the earlier the tumor appeared in embryonic existence, the more marked would

be the bisexuality.

Other workers soon modified Apert's basic conclusion. Lipschutz stated that the adrenals exercise a masculinizing effect on the sex glands. Crosbie and Smith claimed that the cortical cells of the adrenal regulate sexual characteristics such that hypersecretion enhances the action of the testes, and modifies the ovaries toward masculine tendencies. The cortical tumor was considered to be a result of hypersecretion. (31)

In 1921, K. H. Krabbe advanced the interesting theory that during embryonic life the ovary is hermaphroditic, while the testis is monosexual. He claimed that the cortical tissue of the female sex gland was ovarian, but that the medulla was composed of testicular tissue. Later the testicular portion should degenerate. However, Krabbe suggested that this tissue might be absorbed by the adrenals to form a cortex which secretes the male sex hormone, thereby causing the development of male characteristics in the female. Jacobziner and Gorfinkel criticize Krabbe's theory in that it is not substantiated by histological study of embryo tissues. (31)

Müller, 1931, and Klein, 1931, working on rats, found that hypersecretion of the adrenal cortex produces a depressed development of the female gonads, and stimulates the maturation and function of the male sex glands. However, the results have since been proven quite irregular, even to the point where

hyperadrenalism has caused the male to develop female tendencies. Cameron contends that the great lack of uniformity in the results obtained by excess injection of cortical extract prevents the formation of any definite conclusion concerning the interrelation of the adrenals and the sex glands. (58)

Then, in 1933, Dr. Vines discovered that the adrenal cortex reacted positively to a ponceau-fuchsin stain in cases of hermaphroditism and virilism. (31) Further investigation revealed that the stain reacted in all such cases whether a carcinoma was present or not. This discovery indicated that any possible influence of the adrenal must be due to the qualitative nature of the cortical cells rather than to their quantitative structure. (9)

Dr. Vines extended his studies to the fuchsinophilic reaction on embryos. He determined that the adrenal cortex of male fetus's stained strongly between the ninth and seventeenth fetal week, whereas in female embryos the stain showed weaker and its duration was from the eleventh to the fourteenth week. It is worth noting that the first evidence of the fuchsinophilic reaction occurs from two to four weeks after the first signs of sexual differentiation. (9)

Quite recently, experiments by Doctors Broster and Vines have determined that the degree to which the cortical cells react to the ponceau-fuchsin stain varies directly with the secretory activity of the cells. (31) All of which indicates hyperadrenalism has caused the male to develop female tendencies. Cameron contends that the great lack of uniformity in the results obtained by excess injection of cortical extract prevents the formation of any definite conclusion concerning the interrelation of the adrenals and the sex glands. (58)

Then, in 1933, Dr. Vines discovered that the adrenal cortex reacted positively to a ponceau-fuchsin stain in cases of hermaphroditism and virilism. (31) Further investigation revealed that the stain reacted in all such cases whether a carcinoma was present or not. This discovery indicated that any possible influence of the adrenal must be due to the qualitative nature of the cortical cells rather than to their quantitative structure. (9)

Dr. Vines extended his studies to the fuchsinophilic reaction on embryos. He determined that the adrenal cortex of male fetus's stained strongly between the ninth and seventeenth fetal week, whereas in female embryos the stain showed weaker and its duration was from the eleventh to the fourteenth week. It is worth noting that the first evidence of the fuchsinophilic reaction occurs from two to four weeks after the first signs of sexual differentiation. (9)

Quite recently, experiments by Doctors Broster and Vines have determined that the degree to which the cortical cells react to the ponceau-fuchsin stain varies directly with the secretory activity of the cells. (31) All of which indicates a direct relation between adrenal function and virilism. But which is the cause and which the effect?

Grollman claims that the fuchsinophil stain reacts on the androgenic tissue, rather than on the cortical cells. He theorizes that the androgenic tissue should disappear during the first years of post-natal life. Failing this normal degeneration, the tissue continues to elaborate its principles, thereby affecting masculine tendencies in the female. (61)

Additional research with the stain has revealed that a positive reaction can be obtained on the eosinophil cells of the anterior pituitary gland, on the interstitial cells of the testes, and on the peripheral cells of young corpora lutea. This discovery led Cushing, H. M. Evans, and Lescher and Robb-Smith to investigate the pituitary gland. The last three mentioned procured experimental evidence that the pituitary and the adrenal have a coordinated and cooperative function. (31)

Cushing holds that a pituitary adenoma is the basic cause of the chain of glandular malfunctions. He believes that the pituitary disorder causes the adrenal carcinoma, and in turn, both glands disturb the gonadal function. However, investigators have observed that the cortical carcinoma is very frequently found in the absence of any apparent pituitary disorder, consequently, they emphasize the adrenal cortex as the basic affector of the syndrome. But there is still far

too inadequate evidence to draw satisfactory conclusions. (58)

It was found that excess presence of the basophilic cells indicates that the latter are the source of a depressive, inhibitory substance that lowers the metabolism and causes an absence or decrease of sex function. (36)

Lescher and Robb-Smith distinguish between the effects of the pituitary and the adrenal in their claim that the former inhibits gonad function, whereas the adrenal affects a change toward virilism.

M. R. Robinson is of the opinion that the thyroid is also involved in the formation of genital anomalies. His belief is based on several observations of hyperfunctional thyroid glands appearing in conjunction with hyperfunctional adrenals and virilism. (48)

In summary, according to the view of the majority of endocrinologists, hermaphroditism is caused by a multiglandular syndrome involving at least the adrenals, the pituitary, and the sex glands. There is considerable question as to whether the pituitary or the adrenals supply the basic impulse of the multiglandular complex which results in the disturbance of the gonadal function. At present, the majority of investigators believe that the adrenal cortex secretes the basic stimulatory principle. In any case, the degree of maleness in basically female hermaphrodites usually seems to be in direct proportion to the activity of the adrenal cortex.

CORRELATION OF THE CAUSATIVE FACTORS

The geneticists have developed theories to explain the formation of genital anomalies strictly from the point of view of genetics. Stockard and his followers aver definitely that the rate of development is the absolute explanation. And the endocrinologists are equally as positive that the solution to the problem lies in glandular malfunctions.

The views and substantiating arguments of each group may be quite adequate and valid. But perhaps a more complete and inclusive explanation can be found by coordinating and showing the interaction and interdependence of the three suggested causative factors.

Basically the embryo is dependent on its inherited genetic constitution. The morphological and physiological nature of the individual, and also the time and rate of growth and function of the component parts are determined by the genes which the embryo has received.

The rate genes, especially, form a vital factor in creating defects, for, the time of growth of the organs, the time and rate of secretion of the endocrines, and ultimately the metabolic rate depend on the activating powers of these agents. Should the rate genes fail to be coordinated, the

delicate time balance between the crucial stage of development of an organ, and the proper internal environment, as created by the endocrine secretions in regulating the metabolism, will be disturbed. This results in a retardation of the developmental rate, which in turn, probably gives rise to a structural defect.

Faulty coordination of the developmental rates may be due to a lack of balance of gene strength, through an incompatible inheritance, or as a result of chromosomal changes after fertilization. The apparent delicate nature of the chromosomes makes it seem plausible that accidental displacements of the genes, and alterations in the precise chemical nature of these substances may occur. In the event that chromosomes should suffer such effects, the part to be regulated by the effected genes will undergo abnormal development.

Thus it may be seen that the genetic make-up of the organism may be the basic factor which disturbs the coordination between the growth and function of the interdependent organs.

On the other hand, the balance may be destroyed by factors from the external environment. These include mechanical shock, abnormally low temperatures, and most important, chemical affectors. The first two items may alter the metabolic rate by inhibiting the oxidation process. Foreign chemicals may cause a destruction of tissues, or may cause abnormal repression or stimulation of growth or function, thus creating an altered

metabolism, which in turn leads to a disturbance of the developmental rate.

Factors from the external environment generally affect the glands primarily. The genes would not be altered, and the cause of the genital anomalies would be attributable to the endocrines and their resultant influence on the rate of development.

Therefore, it may be concluded that disturbances in the rate of development, morphologically and physiologically, may be considered as the probable vital factor in causing the majority of types of anomalies of the genital organs.

The developmental rate, in turn, is dependent on the genetic constitution and the endocrinological activity. Further, glandular action is affected by genetic factors from within, and by mechanical, physical, and chemical factors from the external environment.

True hermaphroditism is the outstanding abnormality which is probably directly attributable to genetic and glandular influences, one or both, without any apparent relation to a disturbance of the rate of development.

SUMMARY

The female reproductive organs of humans are derived from two main sources. The internal point of origin is the embryonic genital ridge from which develop the ovaries and the Müllerian ducts. These ducts differentiate into paired oviducts, a single fused uterus, and a vagina. The genital groove, the external source, invaginates upward to meet the products of the Müllerian ducts, forming, as it goes, the vulva and probably the lower one-third of the vagina. The genital canal is completed when the invaginated urogenital sinus and the descending products of the Müllerian ducts connect.

The hymeneal membrane, separating the vagina from the vulva is probably derived from the vagina, although some claim it to be a product of the vulva.

The labia minora, developed from the genital folds, the labia majora, from the genital swellings, and the clitoris, produced by the genital tubercle, complete the main parts of the reproductive system.

The anomalies to which the organs of generation are generally subject include absences, rudimentary conditions, multiplicities, displacements, strictures and atresias of the

ducts, atrophies and hypertrophies. Specifically, the individual organs are affected as follows:

The ovaries may be absent or rudimentary, or there may be several ovaries present. The glands are also subject to displacement, cystic formations, and atrophy.

The Fallopian tubes are probably never completely absent, but they may be extremely rudimentary. Like the ovaries, they experience displacements and atrophy. The lumens of the tubes, and the abdominal and uterine orifices are frequently imperforate.

The presence of the uterus, or of some uterine tissue is believed to be constant by many authorities. However, the uterus exhibits many modifications of incomplete development, among which is the absence of the cervix uteri. The majority of uterine defects are the result of incomplete development and fusion of the two Müllerian ducts, or failure of the longitudinal septum between the ducts to disintegrate. Atrophy, hypertrophy, displacements, and obliteration of the ductular passage affect the uterus. The cervical portion and the corpus uteri may be affected independently of each other, except in cases of serious anomalies.

The vagina experiences the same defects as the cervix uteri, and in addition, it may exhibit transverse partitions, and abnormal openings to the exterior.

The hymen is primarily affected through variations in its size and histological structure, and through the size,

number, and shape of its aperture.

The vulva may be absent, rudimentary, or imperforate. The labia majora and minora are frequently subject to hypertrophy, but may also be atrophied. Fusion within, and between the pairs of lips is a recognized anomaly of the labia. There is an apparent absence of the clitoris in cases of extreme epispadias. The erectile organ is also subject to atrophy and hypertrophy.

A final anomalous condition of the female genitals is hermaphroditism. The individual may have testicular tissue and other male organs mixed with the ovaries and basic female parts. Hypertrichosis, change of body contour, and other manifestations of virilism characterize hermaphroditism.

The basic factors causing genital abnormalities are, genetic irregularities, retardation of the developmental rate, and endocrinological malfunctions.

As a result of displacements or chemical changes of the genes, or possibly through polyploidy, there may develop a lack of coordination between the genes for structure and function, and the rate genes, which, in turn, leads to inhibited or abnormal development. Displacements of the sex chromosomes is believed responsible for the development of the male tissues in gynandrists.

Stockard has shown that retardation of the developmental rate during a crucial stage of the early growth of an organ can be responsible for the majority of types of anomalies.

However, Stockard's results have been obtained from experiments on fish, and the application of his conclusions to the explanation of human malformations is purely theoretical and unsubstantiated by experimental evidence.

The endocrines, probably acting through a multiglandular syndrome involving the adrenals, the pituitary, and the sex glands, seem to be a causative factor of genital anomalies. Recent evidence has lead to the hypothesis that hyperfunction of the adrenal cortex is the basic activating factor of the syndrome. However, at least two principles of the basophilic cells of the pituitary gland are known to affect the ovaries, and to stimulate their maturation and secretion of sex hormones.

These three suggested factors seem to be interrelated and interdependent. The developmental rate probably is determined by the genetic constitution, and by the endocrine secretions. The endocrines are regulated by the genes from within, and by chemicals from the external environment.

Thus, a chromosomal change acting directly on the developing tissues, or through the endocrines, or a glandular malfunction activated from the exterior, may result in a retardation of the developmental rate, which may in turn produce anomalous conditions.

Hermaphroditism is probably caused directly by genetic or endocrine disturbances.

BIBLIOGRAPHY

1. Adair, F. L. -- Some Malformations of the Female Genitalia. Journal-Lancet, Vol. 39, 1919, pp 197-205.

2. Archer. -- A Congenital Absence of the Uterus and Vagina. Indian Medical Gazette, Vol. 39, 1904, pp. 412.

3. Arey, L. B. -- Developmental Anatomy. W. B. Saunders Co., 1934, 3rd edition.

4. Bassermann, E. -- Suprarenale und Hermaphroditism. Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie, Vol. 90, 1932, pp. 55-79.

5. Beatty, E. P. -- Two Cases of Absence. Journal of Obstetrics and Gynaecology, Vol. 27, 1920, pp. 145-146.

6. Belson, M. C. -- Imperforate Hymen. American Journal of Surgery, Vol. 36, 1937, pp. 221-225.

BIBLIOGRAPHY

1. Adair, F. L. -- Some Malformations of the Female Genitalia. Journal-Lancet, Vol. 32, 1912, pp 197-203.

2. Archer, -- A Congenital Absence of the Uterus and Vagina. Indian Medical Gazette, Vol. 59, 1924, pp. 412.
3. Arey, L. B. -- Developmental Anatomy. W. B. Saunders Co., 1934, 3rd edition.
4. Basselmann, H. -- Suprarenals and Hermaphroditism. Beiträge zur Pathologischen Anatomie und zur Allgemeinen Pathologie, Vol. 98, 1936, pp. 65-79.
5. Beatty, R. P. -- Two Cases of Absences. Journal of Obstetrics and Gynecology, Vol. 27, 1916, pp. 143-145.
6. Belson, M. O. -- Imperforate Hymen. American Journal of Surgery, Vol. 36, 1937, pp. 221-225.

7. Bovée, J. W. -- The Practice of Gynecology. Lea Bros. and Co., Phila. and New York. 1906.

8. Broster, L. R. -- A Review of Sex Characters--With Special Reference to the Adrenal Cortex. British Medical Journal, Vol. 1, 1931, p. 743.

9. Broster, L. R. -- Eight Years Experience with the Adrenal Cortex. Archives of Surgery, Vol. 34, 1937, pp. 761-791.

10. Cecil, H. L. -- Hypertension, Obesity, Virilism, and Pseudohermaphroditism. Journal of the American Medical Association, Vol. 100, 1933, pp. 463-466.

11. Crew, F. A. E. -- The Genetics of Sexuality in Animals. Macmillan Co., New York, 1927.

12. Cullen, -- Total Absence of the Vagina and Kidneys. American Jounral of Obstetrics, Vol. 62, 1912, p. 296.

13. Cunningham -- Text-book of Anatomy. Edited by Arthur Robinson. Oxford University Press, New York, 1931, 6th edition.

14. Dannreuther, W. T. -- Dextroversion of the Uterus, with Congenital Absence of the Left Fallopian Tube, Ovary, Broad Ligament, Round Ligament, Kidney, and Ureter. American Journal of Obstetrics and Gynecology, Vol. 6, 1923, p. 51.

15. Das, J. M. -- A Case of Congenital Absence of the Vagina with Bilateral Hematosalpinx. Calcutta Medical Journal, Vol. 20, 1926, p. 443.

16. Debierre, Ch. -- Malformations of the Genital Organs of Woman. Translated by J.H.C. Simes. P. Blakiston's Sons and Co., Phila., 1905.

17. Deutschman, D. -- Complete Congenital Absence of the Vagina, Associated with Bilateral Hernias of the Uterus, Tubes, and Ovaries. New York Medical Journal, Vol. 118, 1923, p. 570.

18. Drosin, L. -- Aberrant Ovary and Malformation of the Tube seen in an Operation for Ectopic Pregnancy. Medical Record, Vol. 141, 1935, pp. 95-97.

19. Editorial -- Adrenal Virilism. British Medical Journal, Vol. 2, 1933, pp. 880-881.

20. Emery, F. E. -- Some Aspects of the Anterior Pituitary Sex Hormone on the Weights of the Body, Uterus, Ovaries, Pituitary and Adrenal Glands. Endocrinology, Vol. 17, 1933, pp. 64-71.

21. Ferguson, R. T. -- Absences of the Female Genitalia. Southern Medicine and Surgery, Vol. 99, 1937, pp. 69-70.

23. Findley, P. -- Pregnancy in Uterus Didelphys. American Journal of Obstetrics and Gynecology, Vol. 12, 1926, p. 318.

24. Fitzhugh, O. G. -- Effects of the Cortico-Adrenal Extract on Growth and Sexual Activities. American Journal of Physiology, Vol. 118, 1937, pp. 677-689.

25. Freedman, H. J. -- Disturbances of the Function of the Suprarenal Glands in Children. American Journal of Diseases of Children, Vol. 44, 1932, pp. 1285-1292.

26. Glynn, E. E. -- The Adrenal Cortex--Its Rests and Tumors, Its Relation to other Ductless Glands, and Especially to Sex. Quarterly Journal of Medicine, Vol. 5, 1912, pp. 157-192.

27. Hare, D. C., Ross, J. M., and Crooke, A. C. -- Cortical Carcinoma of the Suprarenal. The Lancet, Vol. 2, 1935, pp. 118-122.

29. Hoskins, R. G. -- Hypergenitalism and Hypogenitalism. Pediatrics, Vol. 4, 1925, p. 745.

30. Hunter, Q. W. --- A Review of the Literature anent Absence of the Uterus and Vagina. Medical Age, Vol. 24, 1906, pp. 603-610.

31. Jacobziner, H., and Gorfinkel, A. -- Familial Congenital Adrenal Syndrome. American Journal of Diseases of Children, Vol. 52, 1936, pp. 308-319.

32. Jones, I. G. -- Sex and Endocrines. Journal of the Arkansas Medical Society, Vol. 33, 1937, pp. 174-179.

33. King, J. E. -- Atresia and Stricture of the Vagina. American Journal of Obstetrics and Gynecology, Vol. 3, 1922, p. 290.

34. Kostmayer, H. W., and Gelpi, M. J. -- Developmental Defects of the Female Genitalia, New Orleans Medical and Surgical Journal, Vol. 65, pp. 573.

35. Lawrence, S. M. -- Vagina Infra Septa, Supra Simplex. British Medical Journal, Vol. 2, 1922, p. 223.

36. Lescher, F. G., and Robb-Smith, A. H. T. -- A Comparison of the Pituitary Basophilic Syndrome and the Adrenal Cortico-Genital Syndrome. Quarterly Journal of Medicine, Vol. 4, 1935, pp. 23-37.

37. Macklin, M. T. -- Heredity as the Cause of Congenital Malformations. American Journal of Obstetrics and Gynecology, Vol. 32, 1936, pp. 258-265.

38. Mall, -- Causes of the Origin of Human Monsters. Journal of Morphology, Vol. 19, 1908.

39. Mall, -- Frequency of Localized Anomalies in Human Embryos. American Journal of Anatomy, Vol. 22, 1917, p. 49.

40. Masson, J.C., and Kaump, D.H. -- A Review of 17 Cases of Interesting Anomalies of the Female Genital Tract. American Journal of Obstetrics and Gynecology, Vol. 33, 1937, pp. 566-576.

41. Miller, G. B. -- Malformations of the Female Genitalia. American Journal of Obstetrics, Vol. 64, 1911, pp. 219-227.

42. Moebius, H. -- Genetics of Sex. Zeitschrift für Menschliche Vererbungs und Konstitutionslehre, Vol. 20, 1936, pp. 254-264.

43. Morgan, T. H. -- Heredity and Sex. Columbia University Press, New York, 1913.

44. Murphy, D. P. -- The Frequency of Conceptions in Families having Congenitally Malformed Children. Surgery, Gynecology and Obstetrics, Vol. 64, 1937, pp. 646-647.

45. Nelson, M. S. -- Congenital Atresia of the Vagina and Imperforate Hymen. Illinois Medical Journal, Vol. 53, 1928, p. 279.

46. O'Farrell, J. M. -- Hereditary Hermaphroditism. Journal of the American Medical Association, Vol. 104, 1935, pp. 1968-1972.

47. Robertson, B. O. -- Absence of the Uterus, Both Tubes, and One Ovary. Southern Medical Journal, Vol. 13, 1920, p. 205.

48. Robinson, M. R. -- Congenital Absence of the Vagina and Uterus. Surgery, Gynecology and Obstetrics, Vol. 31, 1920, pp. 51-53.

49. Rowntree, L. G., and Ball, R. G. -- Diseases of the Suprarenal Glands. Endocrinology, Vol. 17, 1933, pp. 263-294.

50. Scammon, R. E. -- Some Peculiarities of the Growth of the Human Uterus. Anatomical Record, vol. 16, 1919, p. 163.

51. Sinnot, E. W., and Dunn, L. C. -- Principles of Genetics. McGraw Hill Book Co., New York, 1932.

52. Steele, -- Vagina Septate and Bicornate Uterus. Journal of the American Medical Association, Vol. 75, 1920, p. 309.

53. Stockard, C. R. -- Developmental Rate and Structural Expression. American Journal of Anatomy, Vol. 28, 1921, pp. 115-235.

54. Taussig, F. G. -- Discussion of the Article by Dr. King,(33), American Journal of Obstetrics and and Gynecology, Vol. 3, 1922, p.321.

55. Thoinot, L. -- Medicolegal Aspects of Moral Offense. Trans. by A. W. Weysse. F. E. Davis Co., Phila., 1913.

56. Allen, E. -- Sex and Internal Secretions. Williams and Wilkins Co., Baltimore, 1934.

57. Bridges, C.B. -- The Origin of Variations in Sexual and Sex-Limited Characters. American Naturalist, Vol. 56, 1922, p. 51.

58. Cameron, A. T. -- Recent Advances in Endocrinology. P. Blakiston's Son & Co., Phila., Third Edition, 1936.

59. Evans, C.A.L. -- Recent Advances in Physiology. Revised by W. H. Newton, P.Blakiston's Son & Co., Phila., Fifth Edition, 1936.

60. Goldschmidt, R. -- Analysis of Intersexuality in the Gipsy-Moth. Quarterly Review of Biology, Vol. 6, 1931, p. 125.

61. Grollman, A. -- The Adrenals. Williams and Wilkins Co., Baltimore, 1936.

62. Painter, T.S. -- Recent Work on Human Chromosomes -- A Review. Journal of Heredity, Vol. 21, 1930, p. 61.

BOSTON UNIVERSITY
1 1719 02555 0437